THERMAL REARRANGEMENTS OF BICYCLIC *gem*-DIHALOCYCLOPROPANES: THE AROMATIZATION OF 6,6-DIFLUOROBICYCLO[3.1.0]HEX-2-ENE AND 2,3-BENZO-6,6-DIHALOBICYCLO[3.1.0]HEX-2-ENE DERIVATIVES

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TO MOM, LISA, AND HENRIETTE

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By

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Chairman: William R. Dolbier, Jr.
Major Department: Chemistry

The bicyclic gem-difluorocyclopropanes, 6,6-difluorobicyclo [3.1.0]hex-2-ene and 2,3-benzo-6,6-difluorobicyclo[3.1.0]hex-2-ene, have been observed to undergo thermolytic aromatization to give fluorobenzene and 2-fluoronaphthalene respectively. While each process apparently produced analogous aromatic products with competitive activation parameters, this study has demonstrated each thermal rearrangement to proceed via two distinct mechanisms.

The thermal rearrangement of 6,6-difluorobicyclo[3.1.0]hex-2-ene was observed to be a well-behaved, irreversible, first-order process in the gas phase and in solution. The conversion was found to proceed with an activation energy of 27.4 kcal/mol (log A = 11.6) in the gas phase. Near identical activation

energies and log A factors were observed in n-hexane (E_a = 26.3 kcal/mol; log A = 11.5) and acetone (E_a = 25.5 kcal/mol; log A = 11.6). Studies of the thermal rearrangements of 1,2,3,4,4,5-hexadeuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene and endo- and exo-4-deuterio-6,6-bicyclo [3.1.0]hex-2-ene allowed for the determination of a primary kinetic and product-determining (intrinsic) deuterium isotope effect of 2.55 and 1.73 at 93°C respectively. These results demonstrated a mechanism characterized by a rate-determining hydrogen shift.

The thermal rearrangement of 2,3-benzo-6,6-difluorobicyclo [3.1.0]hex-2-ene was characterized as an irreversible, first-order conversion in acetone solution at 150°C. The conversion is marked by a particularly low log A factor in acetone which corresponded to a significant negative entropy of activation (-24.6 eu versus -5.9 eu for acetic acid). A 10^8 rate enhancement was observed in the more polar DMF medium. This result suggested a rate-determining ionization process. Subsequent studies verified this premise.

A study of the thermolysis of a 50:50 mixture of endo and exo-2,3-benzo-4-deuterio-6,6-bicyclo[3.1.0]hex-2-ene in acetone at 150°C produced 4-deuterio-2-fluoronaphthalene and 2-fluoronaphthalene in a ratio of 1.31:1.00 at 20% conversion. The result represented a product-determining deuterium isotope effect of 1.31. This value was found to correlate well with known product-determining H/D isotope effects for eliminations from carbocations.

As control systems, the acetolysis of 2,3-benzo-7,7-difluorobicyclo [4.1.0]hept-2-ene was examined at 200°C. The thermolyses of endo and

exo-6-chloro-6-fluorobicyclo[3.1.0]hex-2-ene, which rearranged to 2-fluoronaphthalene and 2-chloronaphthalene, were studied at 50°C and 150°C in acetone respectively.

CHAPTER 1
THERMAL VINYLCYCLOPROPANE REARRANGEMENTS

Introduction

Studies of thermal carbon-carbon bond breaking processes have led researchers to take advantage of the strain in small-ring hydrocarbons. In this light, thermal isomerization studies of cyclopropane systems have provided insight into the nature of unimolecular homolytic processes. One may include reactions involving diradical mechanisms as well as those arising from electrocyclic or sigmatropic processes as "homolytic." Rates of such reactions generally display little if any solvent effects and proceed at about the same rate in the gas phase as in solution. Therefore, one general observation is the lack of polar characteristics in the transition state.

Substituent effects on the ring cleavage of cyclopropane systems have been intensely studied. Activation parameters have been used to understand the substituent effects and the mechanistic pathways involved in such processes.[1] An example exists in the homolysis of cyclopropane which has an activation energy of about 65 kcal/mol.[2] Attachment of a vinyl substituent introduces a 15 kcal/mol incremental lowering of activation energy (E_a = 50 kcal/mol)[3] solely attributed to transition state stabilization of the incipient diradical. Therefore, the effect of substituents upon the activation parameters of cyclopropane thermal rearrangement processes has been explained in terms of the substituent's ability to stabilize or destabilize an incipient

diradical intermediate (or in the case of concerted sigmatropic or electrocyclic processes the substituent's ability to stabilize or destabilize the transition state).

The effects of fluorine substitution on the ring cleavage of cyclopropane have provided further insight into thermal carbon-carbon bond breaking processes. First, however, one should generalize the effects of fluorine as a substituent.[4]

The properties of fluorine substitution are derived largely from three factors. Fluorine's high electronegativity coupled with its three nonbonded electron pairs explain its unique intrinsic character. As a second period element, it has orbital dimensions that provide excellent overlap in forming strong σ C-F bonds. Also π-conjugative interactions exist with contiguous carbon π systems.

The efficient orbital overlap and fluorine's high electronegativity both contribute to a short, polar C-F σ bond (1.317A relative to C-Cl 1.766A).[5] The effects of fluorine substitution on a variety of organic systems have been documented. In general, introducing fluorine into hydrocarbon systems leads to enhanced thermal stabilization of the carbon skeleton. This stabilization is incremental and may be demonstrated by the following isodesmic reactions.[6]

$$2CH_3CH_2F \longrightarrow CH_3CHF_2 + CH_3CH_3$$
$$\Delta H = -13.1 \text{ kcal/mol}$$

$$3CH_3CHF_2 \longrightarrow 2CH_3CF_3 + CH_3CH_3$$
$$\Delta H = -19.1 \text{ kcal/mol}$$

Figure 1-1. The thermodynamic stabilization of fluorine

In addition, there exists a significant thermodynamic advantage for the fluorine to be bound to carbon orbitals possessing a high degree of p character. An example utilizing the cyclobutene-butadiene equilibrium demonstrates this advantage. In the perfluorinated system, the cyclobutene is more stable.[7]

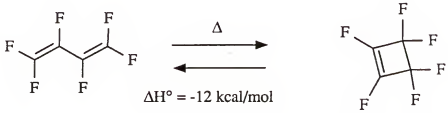


Figure 1-2. Thermodynamic advantage of sp^3-bound flourine substitution

The effect in the thermodynamics of this electrocyclic process may be rationalized by fluorine's electronegativity. It follows that a strong bond would result when fluorine is bound to the less electronegative orbitals of carbon. Also, fluorine's ability as a π donor would create an antibonding interaction involving fluorine's lone pairs with the π system.[4] Abell and Adolf[8] report that a single fluorine stabilizes a π system, a fact verified by Medinger.[9] However, vicinal or higher fluorinated π-substitution affords significant incremental thermodynamic destabilization.

The effect of fluorine substitution on the kinetic stability of cyclopropane provides further interesting consequences which will be discussed here. O'Neal and Benson[10] first commented on the unusual kinetic effects of fluorine

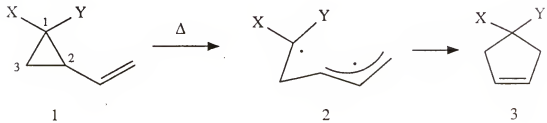
substitution on cyclopropane. In fact, O'Neal and Benson estimated that there is an increase of ring strain of about 5 kcal/mol per fluorine substituent on a cyclopropane ring. Mitsch and Neuvar[11] in an early study suggested that increased fluorine substitution on a cyclopropane ring results in increasing ease of ring cleavage. This observation follows as a consequence of increased ring strain.

Hoffmann and Strohrer[12] and Gunter[13] offered predictions of fluorine's effect on cyclopropane bond strengths. Hoffmann and Strohrer suggested that a potent donor like fluorine should weaken the bond opposite the carbon bearing the fluorine(s) (C2-C3) while the adjacent bonds should be strengthened. Gunter concluded that all cyclopropane bonds should undergo a general weakening. Microwave studies[14] of gem-difluorocyclopropane indicated a shortening of the C1-C2 bond (1.464A) and a lengthening of the C2-C3 bond (1.533A) relative to cyclopropane (1.514A).[15] However, bond lengths cannot necessarily be correlated with bond strengths.[5,16,17] Kinetic studies[5,18,19] of 1,1-difluorocyclopropane systems indicate a general weakening of the carbon-carbon bonds compared to analogous hydrocarbons. Homolysis of the C1-C2 bond is enhanced by 0-2 kcal/mol while the C2-C3 bond homolysis is enhanced by 8-10 kcal/mol.

Vinylcyclopropane Systems

This kinetic effect of geminal fluorine substitution on the thermal rearrangements of vinylcyclopropanes provides a prime example. Flowers and Frey[20] examined the kinetics of the thermal isomerization (Figure 1-3) of the

parent hydrocarbon (vinylcyclopropane 1a) and obtained the activation parameters log A = 13.6 and E_a = 49.7 kcal/mol.

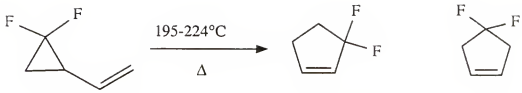


1a X = Y = H
b X = Me Y = H
c X = Ph Y = H
d X = OMe Y = H

Figure 1-3. Thermal isomerization of vinylcyclopropanes

The series of substituents 1b-1d on the vinylcyclopropane all gave the regioselective product 3 which would derive from the homolysis of the C1-C2 bond forming the diradical intermediate 2. The activation energies for the rearrangement via the regiospecific cleavage of C1-C2 are 48.6, 44.7, and 41.0 kcal/mol for 1b-1d respectively.[21,22] A significant rate enhancement was observed for the 1,1-dichloro-2-vinylcyclopropane rearrangement.[23]

A study of the thermal isomerization of 1,1-difluoro-2-vinylcyclopropane showed the interesting kinetic effect of geminal fluorine substitution on cyclopropane.[18]



4 5 6

log A = 13.7 0.96 : 0.04

E_a = 40.3 kcal/mol 85%

Figure 1-4. The thermal isomerization of 1,1-difluoro-2-vinylcyclopropane

The major product 5 was reported, with only 4% of the minor product 6. These results reflect a high degree of regioselective C2-C3 bond cleavage. Fluorine substitution does not appear to provide stabilization to the carbon radical site. In addition, experimental results agree with the earlier-mentioned projections that indicate an incremental energy advantage which involves the selective homolytic cleavage of the bond opposite to the CF_2 group. The log A factor (log A = 13.7) agrees with the parent hydrocarbon system and corresponds to a small positive entropy of activation. This is expected for a homolytic cleavage mechanism of the bond opposite the CF_2 group. Also an incremental lowering of activation energy (ΔE_a = -9.4 kcal/mol) was observed for the rearrangement of 4. It is clear that the major product 5 is formed by a [1,3] sigmatropic process (vinylcyclopropane rearrangement) which is consistent with the involvement of a diradical mechanism.

In contrast, thermal homo[1,5] hydrogen shifts have been observed for various cis-2-alkyl-1-vinylcyclopropanes systems. The thermal isomerization of cis-2-methyl-1-vinylcyclopropane 7 has been described by Ellis and Frey[21] and by Roth and Konig.[22] The process was characterized by a low log A factor (log A = 11.0) corresponding to significant loss of entropy ($\Delta S^{\neq}$ = -11.6 eu) in the transition state. Also the low activation energy (E_a = 31.2 kcal/mol) led to a proposed concerted mechanism for hydrogen transfer and cyclopropane ring cleavage.

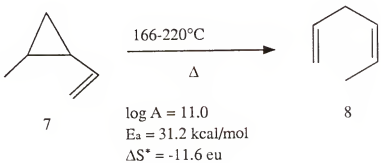


Figure 1-5. Homo[1,5]hydrogen shift process

In comparison, the trans isomer underwent isomerization with activation parameters that were substantially greater than those for the cis isomer. The thermolysis results for the trans isomer 9 are consistent with homolytic cleavage of the cyclopropane ring to give a stabilized diradical that underwent direct cyclization to give the [1,3] sigmatropic shift product 10. In addition, the diradical underwent partitioning via C-C bond rotation followed by rapid hydrogen transfer.

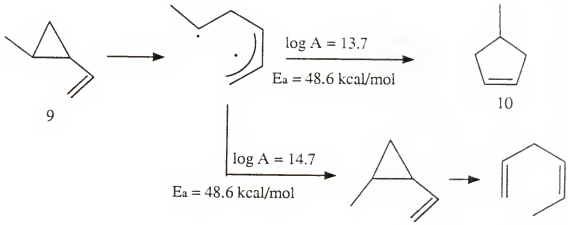


Figure 1-6. Thermal rearrangement of trans-isomer

Kinetic studies of the analogous cis- and trans-2,2-difluoro-3-methyl-1-vinylcyclopropanes 11, 13 showed significant rate enhancements for their rearrangements relative to the hydrocarbon systems.[19] The cis isomer 11 proceeded exclusively via a homo[1,5] hydrogen shift process. The product, cis-3,3-difluoro-1,4-hexadiene 12 was observed in 95% yield. At 100°C, 11 rearranged 6900 times that of the parent hydrocarbon 7 corresponding to a $\Delta\Delta G^{\neq}$ of -9.0 kcal/mol. The trans isomer 13 rearranged to the hydrogen shift product 12 and a major product 14 derived from a [1,3] sigmatropic shift

process. The partitioning in the transition state involving the diradical intermediate afforded a ratio of 14 to 12 of 1.9:1.0.

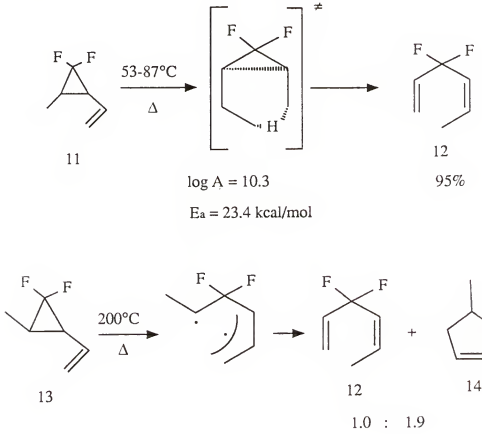


Figure 1-7. Thermolysis of cis- and trans-2,2-difluoro-3-methyl-1-vinylcyclopropanes

Bicyclo[n.1.0]alk-2-ene Systems

A related study, the thermolysis of 8,8-difluorobicyclo[5.1.0]oct-2-ene 15, was examined.[19] This represented an example of a gem-difluorovinylcyclopropane constrained to a bicyclic system. A single product, 3,3-difluoro-1,4-cyclooctadiene 16 was reported at 152.5°C

($k = 4.47 \times 10^{-4}\ sec^{-1}$). Grimme[24] reported a similar process in the bicyclo[5.1.0]oct-2-ene 17 to 1,4-cyclooctadiene 18 rearrangement. The hydrocarbon rearrangement is outlined below (Figure 1-8).

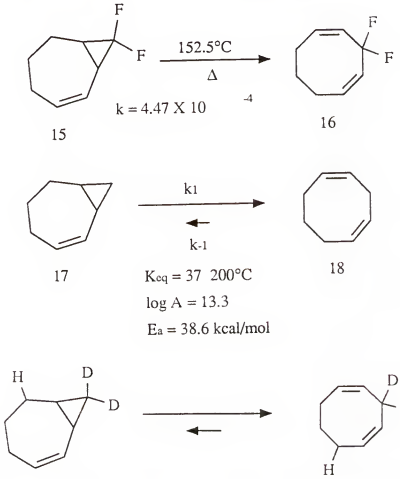


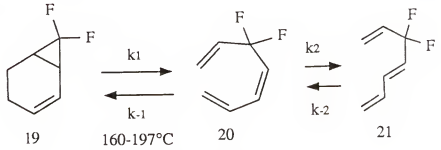
Figure 1-8. Rearrangements of bicyclo[5.1.0]oct-2-ene systems

Also, 8,8-dideuteriobicyclo[5.1.0]oct-2-ene material gives exclusively 3,3-dideutero-1,4-cyclooctadiene. This result would appear to rule out cyclopropane ring opening followed by a vicinal hydrogen shift. Therefore, this observation leaves the homo[1,5] hydrogen shift process as the most reasonable pathway for the conversion of 17 to 18. A relatively low activation

energy for the hydrocarbon system (E_a = 38.6 kcal/mol) leads one to conclude a concerted mechanism is operating since ring opening of vinylcyclopropane requires activation energies of 49-50 kcal/mol via a homolytic process.

A similar process was observed in the difluorobicyclo[5.1.0] system 15. As expected, 15 exhibited a substantial rate enhancement relative to the hydrocarbon system 17. At 152.5°C, 15 underwent its clean homo[1,5]hydrogen shift process 1500 times faster than the hydrocarbon system. This reflects a $\Delta\Delta G^{\neq}$ of -6.1 kcal/mol.

A study relating the interesting mechanistic consequences of a gem-difluorovinylcyclopropane moiety in a bicyclic system has been addressed.[25] The thermal isomerization of 7,7-difluorobicyclo[4.1.0]hept-2-ene 19 displays a retro-Diels-Alder reaction with activation parameters that describe a highly ordered transition state. It was found that 19 underwent a relatively low activation energy thermal equilibrium at 160°C with cis-5,5-difluoro-hepta-1,3,6-triene 20.



k_1: log A = 13.3; E_a = 36.5 kcal/mol
k_{-1}: log A = 9.1; E_a = 28.3 kcal/mol
$\Delta H°$ = +8.26 kcal/mol
$\Delta S°$ = +19.3 eu
$\Delta G°$ = 0.43 kcal/mol

Figure 1-9. The thermal isomerization of 7,7-difluorobicyclo[4.1.0] hept-2-ene

Analysis of the rate clearly shows the more rapid 19=20 equilibrium is >300 times that of the 20=21 equilibrium. Therefore, the formation of 21 may be ignored for the purpose of the kinetic and thermodynamic analysis of the 19=20 equilibrium.

The thermodynamic parameters were determined from a van't Hoff plot of the equilibrium data and are indicated in Figure 1-9. It is apparent that enthalpy favors 19 while entropy factors favor the acyclic heptatriene 20. The entropies of activation clearly show that the transition state for the interconversion process has a structure emulating the bicyclic material 19. For 19 to reach the transition state, very little change in entropy is required ($\Delta S_1^{\neq}$ = -0.4 eu). However, in the reverse reaction, a significant loss of entropy is required to reach the same transition state ($\Delta S_2^{\neq}$ = -19.6 eu).

Unlike the examples of rearrangements involving gem-difluorovinylcyclopropanes previously cited here, the thermal isomerization of 19 has no direct mechanistic analogy in the parent hydrocarbon system. Bicyclo[4.1.0]hept-2-ene is stable at temperatures less than 250°C, and it undergoes rearrangement to a complex mixture of products at 290°C with a half-life of 65 minutes.[26] Clearly, no retro-Diels-Alder acyclic product is observed.

Bicyclo[3.1.0]hex-2-ene System

In the present study, the thermal behavior of 6,6-difluorobicyclo[3.1.0]hex-2-ene 22 and 2,3-benzo-6,6-difluorobicyclo[3.1.0]hex-2-ene 23 has been examined. In a preliminary study,[27] 22 converted smoothly in the gas phase to fluorobenzene 24 at 70°C, while the thermolysis of 23 was

found to give 2-fluoronaphthalene 25. These conversions seemed likely to be related mechanistically. With these reactions having the potential to exhibit new and unusual unimolecular homolytic mechanisms, the present study of 6,6-difluorobicyclo[3.1.0]hex-2-ene systems was initiated.

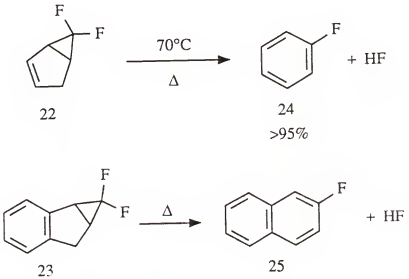


Figure 1-10. Thermal behavior of 6,6-difluorobicyclo[3.1.0]hexene systems

Ellis and Frey[28] first examined the isomerization of the parent hydrocarbon, bicyclo[3.1.0]hex-2-ene 26. At 330°C, 26 converted to a mixture of 1,4- and 1,3-cyclohexadienes (27 and 28 respectively) and benzene. The overall rate of decomposition was first-order. The reaction formally is analogous to the cyclopropane-propene rearrangement and the activation energy correlates well with that expected for the formation of a diradical intermediate with allylic stabilization (E_a = 50.2 kcal/mol). The ratio of 28 to 27 was 1.5, favoring hydrogen migration to the most reactive radical site. The same study

verified that 27 gave benzene and hydrogen via a cis elimination of hydrogen. Orchard and Thrush[29] reported that hydrogen loss from 28 may occur by reversion to 26 then reopening to 27 thus involving the common diradical.

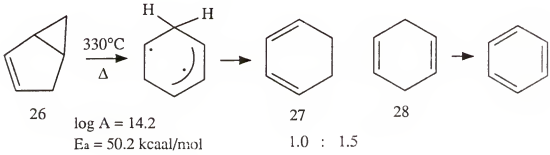


Figure 1-11. Bicyclo[3.1.0]hexene rearrangement

The reversibility of the initial cyclopropane bond homolysis step was demonstrated via the degenerate rearrangement of bicyclo[3.1.0]hex-2-ene which was first observed by Doering and Lambert[30] in the α-thugene system at 200°C. The rearrangement was a result of racemization and deuterium scrambling in the system.

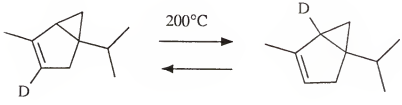


Figure 1-12. Deuterium scrambling in α-thugene

In a later study, Doering and Schmidt[31] provided further insight into the mechanism of the vinylcyclopropane rearrangement constrained to a bicyclo[3.1.0] ring system. Racemization and deuterium scrambling in optically active (-)3,4,4-trideutero-α-thugene 29 were observed to have a log A factor of 14.3 and an activation energy of 43.4 kcal/mol. In addition, the rates of racemization and deuterium scrambling were reported to be nearly equivalent. Two possible diradical intermediates were proposed. One diradical I mirrors the arrangement of atoms in the starting material in which the carbon bearing the isopropyl group lies above the plane formed by the other five carbons in the ring. The other diradical II could be interpreted as deriving from a conformational "ring flip" of the intermediate I.

The pyrolysis of 29 was followed for one half-life (240°C, 196 min, tetraglyme) and the product mixture was examined with respect to deuterium position. Three isomers were present with starting material in different concentrations. In solution, the results are consistent with a suprafacial [1,3] sigmatropic shift with retention of configuration via the non-planar diradical I. This explains the presence of (+)1,7,7-trideutero-α-thugene 30 in 19.4%. The presence of (-)1,7,7-trideutero-α-thugene 31 and (+)3,4,4-trideutero-α-thugene 32 was observed in 8.1% and 7.0% respectively. The formation of 31 and 32 requires a conformational flip of the diradical I to give II which occurs at nearly the same rate as the direct ring closure.

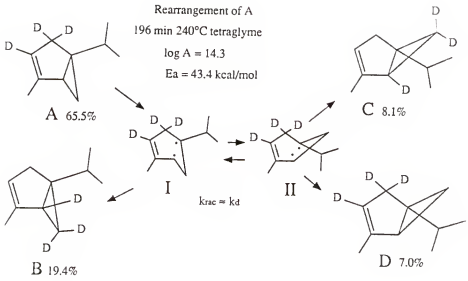


Figure 1-13. The pyrolysis of 3,4,4-trideutero-α-thugene

The major product is formed via a conformationally controled Woodward-Hoffmann orbital symmetry forbidden reaction envoking a 1,3 alkyl shift with retention of configuration.

Conclusion

The thermal rearrangements that occur in nonbicyclic and bicyclic gem-difluorovinylcyclopropanes and in analogous hydrocarbon systems have involved many different mechanistic pathways. In this light, kinetic studies which lead to the determination of activation parameters are excellent methods for elucidation of reaction mechanisms.

The following studies which probe the thermolytic aromatization processes of 6,6-difluorobicyclo[3.1.0]hex-2-ene and 2,3-benzo-6,6-

difluorobicyclo[3.1.0]hex-2-ene rely on closely competitive activation parameters, kinetic and product-determining isotope effects and the thermolysis of model compounds to support the two distinct mechanisms reported in Chapters 2 and 3.

CHAPTER 2
THERMOLYTIC AROMATIZATION OF 6,6-DIFLUROBICYCLO[3.1.0]HEX-2-ENE

Introduction

In a preliminary study Sellers,[27] suggested that 6,6-difluorobicyclo[3.1.0]hex-2-ene underwent a thermolytic aromatization process to produce fluorobenzene as the sole product in high yield. In order to confirm this result and carry out more complete mechanistic elucidation, 6,6-difluorobicyclo[3.1.0]hex-2-ene, 1,2,3,4,4,5-hexadeuterio-6,6-difluorobicylo[3.1.0]hex-2-ene and exo- and endo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene were synthesized and their thermal rearrangements studied.

Syntheses

6,6-Difluorobicyclo[3.1.0]hex-2-ene 22 was prepared in 21% yield from the addition of CF_2 to cyclopentadiene by the method of Wojtowicz using zinc dust and CF_2Br_2.[32] The product 22 was separated and purified by preparative GC. Cyclopentadiene-d_6 was synthesized via an exchange reaction[33] utilizing freshly cracked cyclopentadiene and $NaOD/D_2O$ in DMSO solution. After a total of six exchanges the cyclopentadiene-d_6 was isolated and treated with Zn/CF_2Br_2 to prepare 6,6-difluorobicyclo[3.1.0]hex-2-ene-d_5 33 in 24% yield. Finally exo- and endo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene 34, 35 were prepared by treating cyclopentadiene with $NaOH/TlSO_4$ to afford cyclopentadienyl thallium, followed by hydrolysis[34] with D_2SO_4/D_2O to produce 5-

deuteriocyclopentadiene in good yield. Then, treatment of the selectively deuterated material with the Zn/CF_2Br_2 difluorocarbene reagent provided a 1:1 ratio of the two isomers 34, 35 in modest yield.

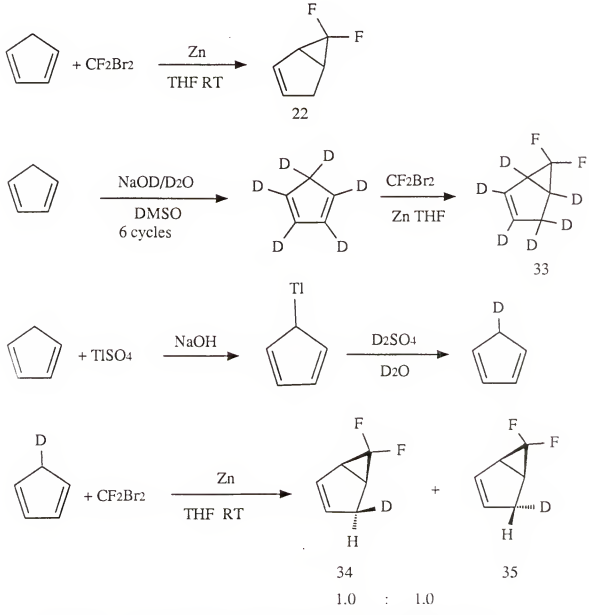


Figure 2-1. Syntheses of 6,6-difluorobicyclo[3.1.0]hex-2-enes

Results and Discussion

The thermolysis of the parent system 22 proved to be well behaved in the gas phase and in solution. The rearrangement is an irreversible, first-order process forming fluorobenzene 24 as the sole product. The kinetic data at various temperatures are presented in Table 2-1. Rate constants at six temperatures in the gas phase and three temperatures each in n-hexane and acetone were determined.

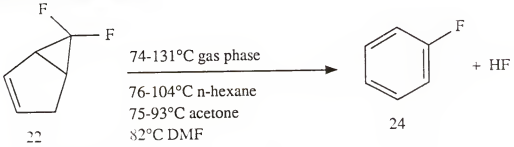


Figure 2-2. Thermolysis conditions

Table 2-1. Rate constants for the conversion of 22 to 24

Solvent	Temp.°C	k X 10^{-5}
gas phase	74.00	0.243(0.004)
	96.00	2.53(0.08)
	105.50	8.09(0.57)
	114.75	14.4(0.6)
	123.25	30.0(0.1)
	131.25	74.8(3.5)
n-hexane	76.0	1.02(0.04)
	93.0	6.20(0.14)
	104.0	17.0(0.7)
acetone	75.0	3.45(0.25)
	82.0	7.42(0.20)
	93.0	21.4(1.6)
DMF	82.0	97.1(6.3)

Table 2-2. Relative rates for the conversion of 22 to 24 at 82.0°C

	gas phase	n-hexane	acetone	DMF
k_{rel}	1.0	3.8	13.7	180

Upon inspection, a gradual rate enhancement was observed for the conversion proceeding from the gas phase to solution. In solution, a very slight increase in rate was apparent with increasing polarity of the solvent. As a point of reference, the reaction proceeds 3.8 times faster in n-hexane than in the gas phase at 82°C. This in not uncommon in that the same unimolecular reaction in solution generally proceeds faster than in the gas phase. Further the $k_{DMF}/k_{acetone}$ is only 13, a result that will be discussed further in Chapter 3. Activation parameters for the conversion of 22 to 24 were determined by a least-squares analysis of the Arrhenius plots of the rate data in the gas phase, n-hexane and acetone.

Table 2-3. Activation parameters for the conversion 22 to 24

Solvent	log A	E_a[a]	$\Delta H^{\neq a,c}$	$\Delta S^{\neq b,c}$	$\Delta G^{\neq a,c}$
gas phase	11.6(0.5)	27.4(0.8)	26.6	-7.83	29.6
n-hexane	11.5(0.3)	26.3(0.5)	25.6	-8.32	28.6
acetone	11.6(0.3)	25.5(0.5)	24.8	-7.94	27.7

[a]kcal/mol [b]cal/deg
[c]109°C/gas phase; 92.0°C/n-hexane; 84.3°C/acetone

It was observed that close similarities exist regarding the activation parameters for the reaction in both the gas phase and solution regardless of solvent. The log A factors are identical within experimental error and they are somewhat lower than those observed in the usual diradical processes (log A = 13.7 for the vinylcyclopropane rearrangement, which corresponds to near zero or slightly positive entropies of activation).[18] A log A factor of 11.5 corresponds to a significant negative entropy of activation ($\Delta S^{\neq}$ = -8.3 eu). The activation energy lowering going from the gas phase to n-hexane and acetone is incremental but the differences are very slight (ΔE_a = 1 kcal/mol). In general, however, the activation energies are also significantly lower than those observed in the parent hydrocarbon systems. The activation energies for bicyclo[3.1.0]hex-2-ene and α-thugene cited earlier were 50.2 (vicinal hydrogen shift) and 43.4 kcal/mol ([1,3] sigmatropic shift/degenerate rearrangement) respectively, each going via a different isomerization process.[28,31]

The activation energies of the homo[1,5] hydrogen shift mechanism are observed to be lower than those reported for diradical processes. Those described for cis-2,2-difluoro-3-methyl-1-vinylcyclopropane 11 and 8,8-difluorobicyclo[5.1.0]oct-2-ene 15 are 23.4 and approximately 32.5 kcal/mol respectively which represents a 7.8 and 6.1 kcal/mol activation energy (ΔE_a) and free energy of activation ($\Delta\Delta G^{\neq}$) lowering respectively with respect to the hydrocarbon systems which react via a homo[1,5] hydrogen shift mechanism (E_a = 31.2 and 38.6 kcal/mol respectively).[19,24]

To further test the pathway of this thermolytic aromatization process,

rates for the conversion of 6,6-difluorobicyclo[3.1.0]hex-2-ene-d_6 33 to fluorobenzene-d_5 36 were determined in the gas phase at three temperatures and in acetone at one temperature. The parent system 22 was allowed to react consecutively in the same well-conditioned vessel.

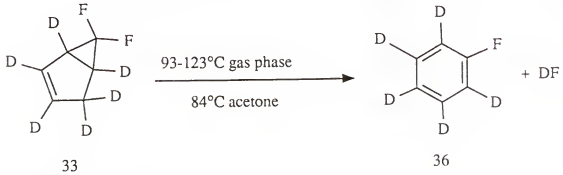


Figure 2-3. Thermolysis of the D_6-system

Table 2-4. Rates and isotope effects for H_6 and D_6 systems

	Temp.°C	k_H X 10^5	k_D X 10^5	k_H/k_D
gas phase	92.80	4.07(0.11)	1.59(0.11)	2.55
	108.00	20.8(0.8)	9.47(0.04)	2.20
	125.75	54.7(0.9)	25.8(1.1)	2.12
acetone	84.0	9.34(0.22)	4.07(0.05)	2.29

These competitive, intermolecular kinetic isotope effects range from about 2.1 to 2.6 displaying a noticeable temperature dependence in the gas phase. In acetone at 84°C, a similar isotope effect was observed. For reference, the deuterium kinetic isotope effect in the [1,5] H-shift of 5-methylcyclopentadiene

and 1,2,3,4,5-pentadeutero-5-methylcyclopentadiene (Figure 2-4) is 5.75 at 27°C.[35] At 100°C, the kinetic isotope effect may be calculated and would be 2.6, verifying a temperature dependence. The relative small magnitude of the observed isotope effect was attributed to a nonlinear transition state for the hydrogen transfer. Also, it should be noted that both primary and secondary deuterium kinetic isotope effects contribute to the observed result. The degree to which secondary effects contribute to the overall observed isotope effect is difficult to conclude. The observed kinetic isotope effects for a homo[1,5] hydrogen shift in the rearrangement observed here at approximately 100°C are not inconsistent with those reported for the model [1,5] H-shift in the methylcyclopentadiene system.

$k_H/k_D = 5.73$ 27°C

calc $k_H/k_D = 2.6$ 100°C

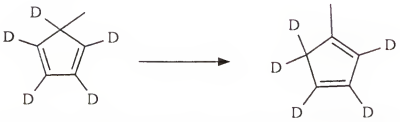


Figure 2-4. Kinetic isotope effect in methylcyclopentadiene

To gain further insight into the details of the rearrangement process the thermolytic aromatization of a 50:50 mixture of the epimeric endo- and exo-4-deutero-6,6-difluorobicyclo[3.1.0]hex-2-enes, 34 and 35, was studied. The reaction was followed by deuterium (^{2}H) NMR. The proton decoupled spectra verified the ratio of starting materials to be 1.0:1.0 (singlets at 2.55 and 2.75 ppm respectively). Following the reaction in acetone solution at 93°C with acetone-d_6 as the internal standard the starting material was found to remain 1.0:1.0 throughout one half-life. Also, conversion of starting material to the aromatic product was followed. Three isomers were observed in the aromatic region corresponding to the ortho-, para- and meta-deuteriofluorobenzenes. The chemical shifts mirrored those observed in the ^{1}H NMR spectrum of fluorobenzene-H_6. The ortho- isomer was a doublet ($^3J_{DF}$ = 1.5 Hz) centered at δ 7.16 ppm. The para-isomer was observed to be a resolved singlet with chemical shift δ 7.23 ppm. Finally, the meta- isomer at chemical shift δ 7.45 ppm was characterized as a broad doublet ($^4J_{DF}$ = 0.9 Hz). At the completion of the reaction, the ratios of the three aromatic isomers were determined by quantitative integration to be 0.81, 0.14 and 0.052 corresponding to the meta-, para- and ortho-deuteriofluorobenzenes respectively.

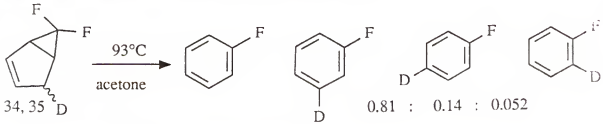
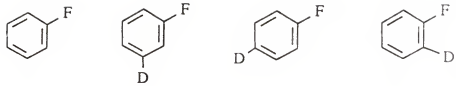


Figure 2-4. D1 study via ^{2}H NMR

There were two interesting results which derived from the ^{2}H NMR study. First, the ratio of the endo- and exo- starting material remained constant at 1.0:1.0 throughout the reaction which indicates that there was no apparent preferential decomposition of one epimer over the other. Second, both para- and ortho-deuteriofluorobenzene products were observed, indicating that hydrogen migration is indeed occurring. In the starting materials, deuterium is in a 1,3 or "meta" relationship to the fluorines. Therefore, all of the meta-deuteriofluorobenzene is derived from H-migration and subsequent HF elimination. The presence of the para-deuteriofluorobenzene can only arise from D-migration to the double bond of the bicyclic starting material followed by subsequent HF loss. Likewise, the ortho-deuteriofluorobenzene must involve D-migration to the cyclopropane side of the bicyclic system followed by extrusion of HF. Obviously, only the deuterated species may be observed by ^{2}H NMR. Clearly D-migration may be followed by rapid DF elimination to afford undeuterated fluorobenzene.

In order to determine the extent to which this process occurred, the NMR mixture of aromatic compounds was submitted for low voltage mass spectrometry (17 eV so as to avoid unnecessary fragmentation processes). Using a spectrum of undeuterated fluorobenzene for calibration, the ratio of deuterated and undeuterated products was determined to be 0.77:0.21 respectively. Finally, the mole fractions of each of the four possible aromatic products could be determined.



0.214	0.634	0.112	0.0405
X_h	X_m	X_p	X_o

$$k_H/k_D = X_m/(X_h + X_p + X_o) = 1.73$$

Figure 2-5. Ratios of aromatic products

An intramolecular isotope effect k_H/k_D (based on product determination) for the H-migration process could be calculated by the equation indicated in Figure 2-5. This value is 1.73. The result is undoubtedly primary, though small in magnitude. This effect represents the intrinsic primary isotope effect for the hydrogen shift process. Recall that the kinetic isotope effect at 93°C in the gas phase was 2.55.

While the observed kinetic and intrinsic isotope effects are not the same, we, nevertheless, propose that they represent the same reaction step. In an intermolecular competition, an isotope effect will only be observed if the H-shift occurs in the rate-determining step. In contrast, in an intramolecular isotope effect determination, the full value of k_H/k_D would be observed regardless of whether the H-shift occurs in the rate-determining step or a subsequent fast step.

Proper consideration of secondary deuterium isotope effects is necessary

to elucidate the mechanistic conclusion. Dolbier and Alonso[36] and Melander and Saunders[37] report secondary α-deuterium isotope effects for diradical and solvolysis processes to be about 1.1 per deuterium. In addition, Melander and Saunders[37] conclude that secondary β-deuterium isotope effects are also approximately 1.1 per deuterium in solvolyses. In 1,2,3,4,4,5-hexadeuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene 33 a total of two alpha- and two beta-effects are present ($1.1^4 = 1.46$). The corrected value for the intermolecular k_H/k_D (2.55/1.46) is 1.8. In addition, there is also a secondary effect accelerating k_D relative to k_H in exo- and endo-4-deuterio-6,6-bicyclo[3.1.0]hex-2-ene 34 and 35. Using the correction (1.73 X 1.1), a value of 1.9 is obtained. The magnitude of the calculated inter- and intramolecular isotope effects following the appropriate corrections for secondary deuterium isotope effects is essentially the same within experimental error; and therefore, it seems reasonable that they represent the same mechanistic step.

We conclude from both sets of data that the hydrogen transfer process would appear to be rate determining with nonlinear transfer of hydrogen in the transition state. The angle of hydrogen transfer affects the magnitude of observed primary deuterium isotope effects. The optimum 180° (linear) transfer of hydrogen gives rise to the most pronounced primary isotope effects. In addition, it follows that the degree of bond formation at the transition state is not equal to the degree of bond breaking. Therefore, the transition state may be reactant or product-like and not "symmetrical."[38]

Finally, the epimeric starting materials, as alluded to earlier, undergo

reaction without a noticeable difference in rate. One might expect there would be some selectivity in the decomposition of starting materials. The lack of such selectivity suggests that a pre-equilibrium must be occurring involving the epimerization of the starting materials, that is followed by rate-determining hydrogen transfer which may be referred to as a homo[1,5] hydrogen shift process. What is not clear is whether the epimerization is on the same energy surface as the apparent homo[1,5] shift. In view of the fact that both ortho- and para-deuteriofluorobenzene products are formed, it would appear that the H-shift occurs via the diradical--a process analogous to the cyclopropane-propene rearrangement (or vicinal 1,2 shift) process.

If the diradical mechanism were operating, one might expect more ortho-isomer to be produced from H-migration to the reactive secondary radical site (compared to the stabilized allylic radical). Dolbier and Al-Fekri[39] observed an inhibition of the 1,2-hydrogen shift process from an intermediate 4,4,5,5-tetrafluorobicyclo[2.1.0]pentane-1,3-diyl species relative to the analogous hydrocarbon system. The fact that we observe H-migration away from the fluorines to the hydrocarbon (allylic radical) side preferentially (para/ortho = 2.7) would qualitatively corroborate an inhibition to 1,2 H-migration caused by the fluorines.

Recall that the activation energy for the hydrogen shift in 6,6-difluorobicyclo[3.1.0]hex-2-ene 22 was 27.4 kcal/mol in the gas phase. It is not possible to predict such a low activation energy for diradical formation. In fact, it is impossible to calculate an activation energy below 35 kcal/mol for the

diradical forming process. Nevertheless, one is constrained to assume exo-endo interconversion of starting material. A qualitative report[40] provides the best example of a rapid thermal interconversion process of the endo and exo difluorocarbene adducts of norbornadiene at 60°C.

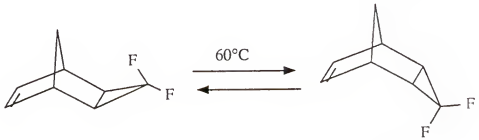


Figure 2-6. Facile thermal interconversion process

Conclusion

The mechanistic scheme for the thermolytic aromatization process observed in the conversion of 6,6-difluorobicyclo[3.1.0]hex-2-ene to fluorobenzene appeared to be consistent with the involvement of a rate-determining homo[1,5] hydrogen shift. The deuterium NMR results suggested a pre-equilibrium involving the epimerization of the endo and exo starting materials. The hydrogen shift process would follow (k_2). The two 1,3- and 1,4-cyclohexadiene reactive intermediates, which were not observed, apparently aromatized rapidly via thermal extrusion of HF. A gas sample was collected at

one half-life, and it was subjected to a low-temperature ^{19}F NMR experiment from -60°C to room temperature. Only bicyclic starting material and product (fluorobenzene) were observed.

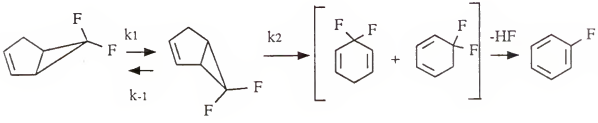


Figure 2-7. Mechanism of parent system rearrangement

CHAPTER 3
THE THERMOLYTIC AROMATIZATION OF 2,3-BENZO-6,6-DIHALOBICYCLO[3.1.0]HEX-2-ENE DERIVATIVES

Introduction

It was considered likely that 2,3-benzo-6,6-difluorobicyclo[3.1.0]hex-2-ene 23 would undergo a similar thermolytic aromatization process to produce 2-fluoronaphthalene 24. In order to confirm this hypothesis and elucidate a contrasting mechanism (from that discussed in Chapter 2), 2,3-benzo-6,6-difluorobicyclo[3.1.0]hex-2-ene, 2,3-benzo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene, 2,3-benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene and endo- and exo-2,3-benzo-6-chloro-6-fluorobicyclo[3.1.0]hex-2-ene were synthesized and their thermal rearrangements studied.

Syntheses

Seyferth and Hopper's method[41] was used to synthesize the system 23. Freshly distilled indene was treated with vacuum-dried $PhHgCF_3$ and NaI in refluxing benzene for 15 hours. The adduct 23 was isolated in good yield (45%) and was purified by preparative GC as a low melting solid (mp 35-38°C). Deuterium labeled indene-d, was prepared 81% pure by treating indene with n-butyllithium and then with D_2O/DCl via inverse addition. A 1:1 mixture of the endo and exo-2,3-benzo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene was prepared via the Seyferth difluorocarbene reagent. The model compound 2,3-

benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene 37 was also prepared by difluorocarbene addition to dihydronaphthalene.

The nonbicyclic model system trans-1,1-difluro-2-methyl-3-phenylcyclopropane 38 was synthesized from trans-β-methylstyrene using Wojtowicz's[32] Zn/CF_2Br_2 reagent. Finally, endo- and exo-2,3-benzo-6-chloro-6-fluorobicyclo[3.1.0]hex-2-ene 39, 40 were prepared in a 2.3:1.0 ratio using $CFCl_3$, $TiCl_4$ and $LiAlH_4$ in THF at 0°C.[42]

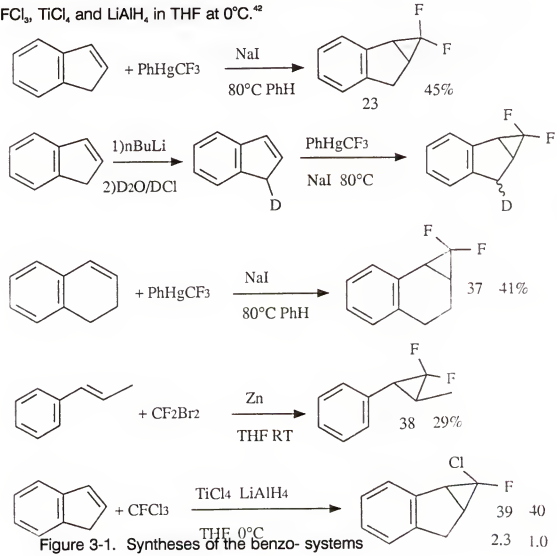


Figure 3-1. Syntheses of the benzo- systems

Results and Discussion

The rates of thermal conversion of 23 to 2-fluoronaphthalene 25 were determined in acetone (five temperatures), acetic acid (three temperatures), n-heptane and DMF (one temperature each) with the results given in Table 3-1.

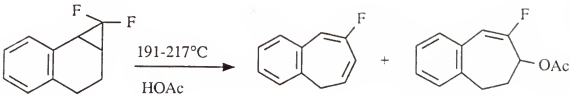
Table 3-1. Rate constants for the conversion of 23 to 25 in solution

Solvent	Temp.°C	k X 10^{-5}
acetone	140.0	1.71(0.08)
	150.0	3.32(0.14)
	160.0	6.42(0.05)
	170.0	12.1(0.5)
	180.0	23.1(0.5)
acetic acid	81.0	2.49(0.05)
	100.0	16.5(0.4)
	119.0	102(2)
n-heptane	186.0	5.82(0.16)
DMF	70.0	0.866(0.012)

When the rates were compared, it was apparent that there was a very significant solvent effect in this reaction. A rate enhancement of ~~5.4 X 10^{4}~~ 408 was observed at 70°C for the more polar DMF medium compared to acetone. This result suggests a rate-determining ionization process. As a point of reference, the $k_{DMF}/k_{acetone}$ at 82°C for the parent system (Chapter 2) was only 13.

As a control system, 2,3-benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene 37 was examined. This system was stable in acetone solution at 200°C, however 37 did undergo acetolysis and rate constants for this process were determined

at three temperatures (191-217°C).



37

Figure 3-2. Acetolysis of 2,3-benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene system

Table 3-2. Rate constants for the acetolysis of 37

Temp, °C	191.0	204.0	217.0
k X 10^{-5}	0.939(0.019)	2.95(0.04)	8.28(0.19)

The rearrangement of 37 was followed by ^{19}F NMR spectroscopy with hexafluorobenzene as an internal standard. Two products, the HF elimination product and the acetate were observed. At 217°C, 37 underwent thermal rearrangement in acetic acid 11,000 times slower than 23.

The acetolysis of other model gem-difluorocyclopropane systems were examined. The styrene adduct, 1,1-difluoro-2-phenyl-cyclopropane, was relatively stable to treatment with acetic acid at 217°C. However, the methyl substituted system, trans-1,1-difluoro-2-methyl-3-phenylcyclopropane 38, underwent smooth rearrangement at 217°C in acetic acid. The rate constant for the ring-opening was 1.46(0.06) X 10^{-4}, 1.8 times faster than 37.

The thermolyses of endo- and exo-2,3-benzo-6-chloro-6-

fluorobicyclo[3.1.0]hex-2-ene 39, 40 were studied at three temperatures in acetone (39-64°C and 140-160°C respectively). The rearrangements were followed by ^{19}F NMR in the presence of hexafluorobenzene as the internal standard. The endo-chloro compound 39 afforded 2-fluoronaphthalene while the exo-chloro system 40 rearranged solely to 2-chloronaphthalene.

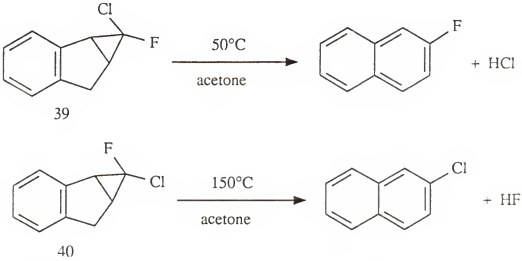


Figure 3-3. Thermolytic aromatization of chloro-fluoro systems

Table 3-3. Rate constants for chloro-fluoro-systems in acetone

Compound	Temp.°C	k X 10^{-4}
endo 39	140.0	2.81(0.09)
	150.0	6.15(0.13)
	160.0	11.8(0.38)
exo 40	39.0	0.234(0.005)
	51.0	1.08(0.02)
	64.0	5.42(0.19)

Activation parameters were obtained from the rate data for all of the benzo- systems presented here.

Table 3-4. Activation parameters of 2,3-benzo- systems

Cpd	Solvent	log A	Ea	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$	Temp
23	acetone	8.0(0.1)	24.2(0.3)	23.3	-24.6	34.0	160.
	HOAc	12.0(0.3)	27.0(0.5)	26.2	-5.9	28.4	99.7
37	HOAc	12.8(0.3)	37.9(0.6)	36.9	-2.9	38.3	204
39	acetone	13.8(0.2)	26.3(0.3)	25.7	+2.3	24.9	51.0
40	acetone	10.0(0.3)	25.6(0.5)	24.7	-15.6	31.3	151
			kcal/mol	kcal/mol	eu	kcal/mol	

The conversion of the 2,3-benzo-6,6-diflurobicyclo[3.1.0]hex-2-ene system 23 to 2-fluoronaphthalene 25 is marked by a particularly low log A factor in acetone which corresponds to a substantial negative entropy of activation ($\Delta S^{\neq}$ = -24.6 eu versus -5.9 eu for acetic acid). The entropies of activation for solvolysis processes have been demonstrated in earlier studies to be solvent dependent and often negative.[43] In contrast, the simple homolytic cleavage of gem-difluorocyclopropanes cited in Chapter 1, exhibited near zero to small positive entropies of activation as might be expected for diradical-forming reactions. Also, it is interesting to note that the energies of activation are not drastically different in spite of large rate differences (24.2 and 27.0 kcal/mol in acetone and acetic acid respectively). At 100°C, the conversion proceeds 300 times faster in acetic acid which corresponds to a $\Delta\Delta G^{\neq}$ of -5.6 kcal/mol. Activation energies for

the vinylcyclopropane rearrangement and other thermal homolytic processes are significantly higher. Moreover, analogous mechanisms invoking a [1,3] sigmatropic rearrangement or a homo[1,5] hydrogen shift for the 23 to 25 conversion would disrupt aromaticity in fused benzene ring, a high energy process. In addition, the best guess of the energy required for simple homolytic cleavage of the bridge-head C-C bond in 23 is not less than 35 kcal/mol.

A related study involved the conversion of a 1:1 mixture of endo and exo-2,3-benzo-4-deutero-6,6-difluorobicyclo[3.1.0]hex-2-ene 41, 42 to a mixture of 4-deutero-2-fluoronaphthalene and 2-fluoronaphthalene. The reaction was observed at 150°C in acetone solution and the recovered starting materials were analyzed by ^{1}H NMR and the aromatic products were analyzed by low-voltage mass spectrometry. The ratio of starting materials remained 1:1 throughout the reaction (analyzed at 20 and 50% conversion). At 20% conversion, a primary product-determining isotope effect of 1.31 was observed. A ^{2}H NMR spectrum of the products confirmed the presence of 4-deuterio-2-fluoronaphthalene as the only deuterated product. No products from possible deuterium migration were observed.

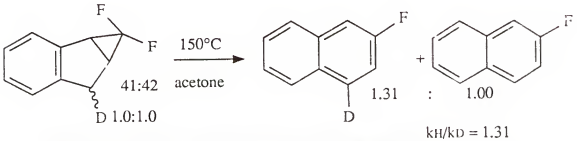


Figure 3-4. Product-determining isotope effect study

Product-determining primary H/D isotope effects for elimination from carbocations have been documented.[44] The range for E_1 primary effects run from about 1.4-2.0 (at 20% conversion).

An interesting contrast was observed in relating the acetolysis reactions of the [3.1.0] system 23 and the [4.1.0] system 37. At 217°C 23 rearranged 11,000 times faster than 37. This corresponds to a $\Delta\Delta G^{\ddagger}$ of -9.9 kcal/mol. This significant difference in activation energies can be rationalized as a reflection of the relative release of strain expected in the transition states for the two ionization processes. In this light, such a difference may be solely attributed to the ring strain present in the two systems and not due to any "special" mechanism for the [3.1.0] system.

An approximate quantitative view of ring strain is possible by choosing appropriate models. Bicyclic ring strain is approximated by adding the strain energies in each ring.[17] The strain energy of 1,1-difluorocyclopropane is about 34.4 kcal/mol or 6 kcal/mol more than cyclopropane (28.3 kcal/mol).[45] The strain energy in cyclopentene is 6.9 kcal/mol.[17] The additive effect in the bicyclo[3.1.0]hexene system would result in a strain energy of 41.3 kcal/mol. The bicyclo[4.1.0]heptene system has a calculated strain energy of 37.0 kcal/mol (2.6 kcal/mol for cyclohexene plus 34.4 kcal/mol for 1,1-difluorocyclopropane). This difference in ground state strain energies is approximated at 4.3 kcal/mol (ΔE_s).

At the transition state, the [3.1.0] system is opening to a less strained 6-membered ring (E_s = 2.6 kcal/mol for cyclohexene). The [4.1.0] ring-opening

involves formation of a 7-membered ring (E_s = 7.0 kcal/mol for cycloheptene).[17] Cyclohexene and cycloheptene were used as models since information on cyclic diene ring strain is somewhat scarce. This estimated difference at the two transition states is 4.5 kcal/mol ($\Delta E_s^{\neq}$). The total relief of strain at the transition state of the two systems may be expressed by ΔE_s + $\Delta E_s^{\neq}$. This sum is about 9 kcal/mol for the two processes.

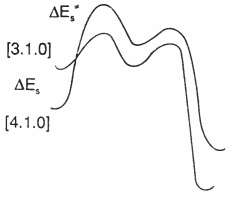


Figure 3-5. Relative energy diagrams of [3.1.0] vs [4.1.0]

The chloro-fluoro- systems may also be examined as potential model compounds undergoing rate-determining ring-opening ionization processes. Both processes involve ionization of the endo halogen synchronous with ring opening. Classic studies by de Puy et al.[46] and Schleyer et al.[47] demonstrated cyclopropane solvolyses to be stereospecific, two-electron processes involving concerted ionization and disrotatory C2-C3 cyclopropane bond fragmentation. In bicyclo[3.1.0] systems, the allyl cation that is produced by the Schleyer mechanism would be a <u>trans</u>-cyclohexenyl cation which is considerably strained.

This is evident in the bicyclic tosylates where the endo-epimer reacts 2 X 10^8 times faster.[48]

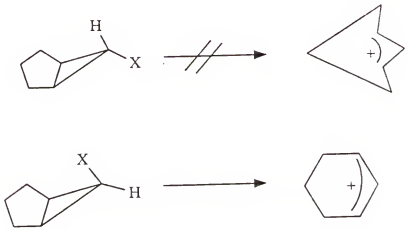


Figure 3-5. Solvolysis of bicyclic tosylates

The activation energies for the endo and exo-chloro (39 and 40) are virtually the same (Ea = 26.3 and 25.6 kcal/mol respectively). However, the rate ratio k_{endo}/k_{exo} of 1800 ($\Delta\Delta G^{\neq}$ = -6.4 kcal/mol) is largly entropy driven. The log A factors of 13.8 for the endo-epimer and 10.0 for the exo-epimer correspond to entropies of activation of +2.3 and -15.6 eu respectively. A positive entropy is associated with the ring-opening ionization of chloride in the endo-epimer and significant negative entropy accompanies the loss of fluoride ion from the exo-epimer. As a point of reference, the entropy of activation

observed in the thermolysis of the difluoro system 23 was -24.6 eu. This result quantifies the free energy of activation difference ($\Delta\Delta G^{\neq}$) in chloride versus fluoride leaving in this specific bicyclic system.

Conclusion

The thermolytic aromatization of 2,3-benzo-6,6-difluorobicyclo[3.1.0]hex-2-ene, which occurs smoothly in a variety of solvents, appears to involve a mechanism reminiscent of those previously observed for gem-dihalocyclopropane solvolyses.[49]

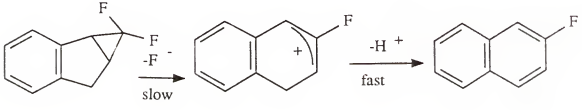


Figure 3-6. Aromatization mechanism of 23

The model systems presented here and their analogous thermal rearrangements provided support for and offered keen insight with respect to relative ring strain and leaving group effects on the ionization process.

CHAPTER 4
EXPERIMENTAL SECTION

General Methods

Nuclear magnetic resonance (NMR) chemical shifts are reported in parts per million (ppm) downfield (δ) from internal reference TMS for ^{1}H and ^{13}C spectra, and as o, ppm upfield for $CFCl_3$ in the case of ^{19}F spectra. Acetone-d_6 was used as an internal reference for ^{2}H spectra. All NMR spectra were acquired on a Varian VXR-300 instrument. Mass spectra and exact masses were determined on a Kraytos/AEI-MS 30 spectrometer at 70 eV unless otherwise noted.

Chromatographic separations were performed by gas-liquid chromatography (GLC). Preparative GC utilized a Varian Aerograph A90-P3 gas chromatograph with a thermal conductivity detector.

Kinetics runs were performed either on a Hewlett-Packard 5710A gas chromatograph equipped with a flame ionization detector and an attached HP 3380S Integrator or integration of the appropriate NMR spectra using the Varian VXR-300.

Starting material and product ratios were determined in most cases with an appropriate internal standard. Three successive GC injections or NMR integrations were averaged.

Experimental Procedures

6,6-Diflurobicyclo[3.1.0]hex-2-ene (22).[32]

A 100 ml 3-necked round bottom flask was equipped with a magnetic stirrer, thermometer, rubber septum with N_2 inlet needle and a pressure-equalizing addition funnel. The system was flushed with N_2 and 10 ml of dry THF, 1.49g (22.8mmol) activated zinc and 0.50g (7.6mmol) of freshly cracked cyclopentadiene was added. In addition a small crystal of iodine was added. The addition funnel was charged with 4.79g (22.8mmol) of CF_2Br_2 in 10 ml THF. The CF_2Br_2 was added over a 1.5-2 hour period slowly with the reaction temperature not exceeding 30°C. After addition the mixture was allowed to stir for one hour at room temperature as the zinc was slowly consumed. The reaction mixture was then washed twice with water and the organic layer was separated. The ^{19}F NMR yield was 21% using hexafluorobenzene as the internal standard. The product 22 was separated and purified by preparative GC using a Triton X-305 column at 50°C/60 psi. A total of 425mg was collected.

6,6-difluorobicyclo[3.1.0]hex-2-ene (22): ^1H NMR (300 MHz), δ 5.72 (complex m, 1H, olefinic), 5.63 (m, 1H, olefinic), 2.82-2.58 (complex m, 3H, -CH_2-, cyclopropyl H), 2.20 (m, 1H, cyclopropyl H); ^{19}F NMR, o = -155.7 (d, $^2J_{FF}$ = 146.8 Hz); -129.4 (ddd, $^2J_{FF}$ = 146.5 Hz, $^3J_{cisHF}$ = 12.8 Hz, $^3J_{cisHF}$ = 11.1 Hz); mass spectrum, m/z (% relative intensity) 116 (M^+, 1.93), 96 (9.72), 64 (22.76), 46 (100.00).

Thermal Rearrangement of 6,6-difluorobicyclo[3.1.0]hex-2-ene (22).

6,6-Difluorobicyclo[3.1.0]hex-2-ene (60.0mm) was expanded into a well-conditioned pyrolysis bulb and pyrolized at six temperatures between 74.00 and 131.25°C. An internal standard benzene was added (15.0mm). The reaction was followed by GC with a 2 ft. x 1/8 in., CARBOPACK C column at 50°C. The raw kinetic data are listed in Table 4-1 while the rate constants are given in Table 2-1. The pyrolysis afforded fluorobenzene as the sole product, easily distinguishable its ^{19}F NMR.

Fluorobenzene (24): ^{19}F NMR, o = -113.6 (dd, $^{3}J_{HF}$ = 7.5 Hz).

Solution Kinetics Procedure for the Thermolysis of (22).

The kinetic vessels were sealed 507 NMR tubes. In each tube was placed approximately 10mg of 22, along with 0.5ml acetone-d_6 and 2ul of an internal standard hexafluorobenzene was syringed into the solution. New samples were prepared for each temperature. For the n-hexane solution run, samples were prepared in a similar mannar except n-hexane with 0.1ml C_6D_6 represented the solution media. Finally, the DMF run utilized acetone-d_6 as the deuterated solvent. A statim-type isothermal heater was used to pyrolyze the tubes in the temperature range 75.0-104.0°C depending on the solvent. At designated time intervals, the tubes were cooled to -50°C and the raw kinetic data (Table 4-2) were determined by quantitative ^{19}F NMR integration of starting material and product. Rate constants are reported in Table 2-1.

1,2,3,4,5,5-hexadeuteriocyclopentadiene.[33]

At 0°C a $NaOD/D_2O$ solution was prepared by adding 8.4g of Na to D_2O slowly. Into a 100ml round bottem flask equipped with a stir bar, rubber septa and cooled to 0°C was added 18ml of freshly cracked cyclopentadiene and 20ml of DMSO. To this organic mixture, 20ml of the $NaOD/D_2O$ solution was added. The mixture was stirred vigorously for one hour, and an intense pink color was observed during the exchange. The top, cyclopentadiene layer was separated and syringed into another 100ml flask containing 20ml each of fresh DMSO and $NaOD/D_2O$ solution at 0°C. This procedure was repeated 6 times (6 exchanges) and ^1H NMR confirmed deuteration to >95%. Approximately 7ml (39%) of the desired product was isolated and utilized immediately.

1,2,3,4,4,5-hexadeuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene (33) .[32]

The procedure for the preparation of 33 is analogous to that of the parent system 22 previously described. Into the standard apparatus was placed 1.0g (13.9mmol) of the freshly prepared cyclopentadiene-d_6 and 2.73g (41.7mmol) activated Zn dust in 10ml dry THF. To this stirred mixture, 8.8g (41.7mmol) CF_2Br_2 in 15ml THF was slowly added over a two hour period. The ^{19}F NMR yield was 24%.

1,2,3,4,4,5-hexadeuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene (33): ^{19}F NMR, o = -129.2 (d, $^2J_{FF}$ = 148.2 Hz); -155.4 (d, $^2J_{FF}$ = 148.0 Hz); mass spectrum, m/z (relative intensity) 122 (M^+, 8.02), 120 (M - 2, 100.00), 101 (6.35), 72 (19.96).

Thermal Rearrangement of (33).

1,2,3,4,4,5-Hexadeuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene (80.0mm) was expanded into the same well-conditioned pyrolysis bulb and pyrolyzed at three temperatures between 92.80 and 125.75°C. Benzene was added (15mm) as an internal standard. The parent (H_6) system 22 (80.0mm) was pyrolyzed in the same vessel and temperature immediately following the pyrolysis of 33. The GC analysis of starting material and internal standard produced the raw kinetic data reported in Table 4-3. The rate constants and kinetic isotope effect data are listed in Table 2-4. The acetone solution kinetic run was monitored at 84.0°C in the same way as the previous solution runs with the parent system 22. Once again, 22 was pyrolyzed and analyzed in addition to 33. Quantitative ^{19}F NMR integrations provided the raw kinetic data also presented in Table 4-3. The rate constants and the solution isotope effect is found in Table 2-4.

2,3,4,5,6-pentadeuteriofluorobenzene: mass spectrum, m/z (% relative intensity) 101 (M^+, 100.00).

5-Deuteriocyclopentadiene.[34]

In a 125ml Erlenmyer flask with a stir bar, 6.0g (0.091mol) freshly cracked cyclopentadiene, 30ml 4N NaOH and 10.08g (0.020mol) Tl_2SO_4 were allowed to react for a short time. The crude product cyclopentadienyl thallium (10.5g: 80.0%) was collected by filtration. The crude cyclopentadienyl thallium was sublimed pure (0.6atm, 105°C) to give fine yellow needle-like crystals. The

hydrolysis went smoothly using a standard 3-necked round bottom flask equipped with a magnetic stir bar and a pressure-equalizing addition funnel. The apparatus, under nitrogen flow was kept at room temperature. Three traps (ice, dry ice/iPrOH and liquid nitrogen) were placed in series. Into the reaction flask, 3.09g (11.5mmol) cyclopentadienyl thallium was added, and the addition funnel was charged with 2ml 10% D_2SO_4. The product, 5-deuteriocyclopentadiene, was collected (0.5g, 40%) in the dry ice trap. The material was kept at -78°C and used directly for the carbene addition. Purity was checked by ^{1}H NMR and integration of the material verified the structure (4:1, vinylic:methylene).

exo and endo-4-Deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene 34, 35.[32]

As before, in the standard apparatus, 1.00g (8.5mmol) of 5-deuteriocyclopentadiene in 10ml THF was added to 1.67g (25.5mmol) zinc in the reaction flask. To this mixture, 5.35g (25.5mmol) CF_2Br_2 in 15ml THF was slowly introduced. The ^{19}F NMR yield was 19%. Approximately 100mg was isolated by preparative GC at 50°C and 60psi with the detecter and injector temperature at 50°C to gard against rearrangement. A Triton X-305 column was used, and both epimers were collected together.

exo and endo-4-Deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene (34),(35): ^{1}H NMR δ 5.71 (m, 1H, olefinic), 5.62 (m, 1H, olefinic), 2.66 (complex m, 2H, -CHD + cyclopropyl), 2.19 (complex m, 1H, cyclopropyl); ^{2}H NMR δ 2.75 (s, 1D), 2.53 (s, 1D), each δ represents one epimer; ^{19}F NMR o = -129.3 (ddd?, $^2J_{FF}$ = 147.0 Hz, $^3J_{cisHF}$ = 11.6 Hz), -155.7 (d, $^2J_{FF}$ = 147.0 Hz).

Thermolysis of (34) and (35).

The pyrolysis in acetone solution of a 50:50 mixture of the two epimers was followed in a sealed 507 NMR tube by ^{2}H NMR. The tube was heated in a Statim-type oil heater at 93.0°C, cooled to -50°C and analyzed by NMR with acetone-d_6 as an internal standard. The raw kinetic data from the run are included in Table 4-4. The reaction was allowed to proceed for approximately 6 half-lives and the aromatic product mixture was isolated by preparative GC from the NMR tube. All three (m, p and o) monodeuteriofluorobenzene isomers were present by ^{2}H NMR in a ratio of 80.6:14.2:5.2 respectively. The purified aromatic mixture was submitted to mass spectrometry (17eV). A pure sample of fluorobenzene provided the reference spectrum. The MS absolute intensities and ^{2}H NMR ratios were used to calculate the mole fractions of the four products (Figure 2-5).

Fluorbenzene: mass spectrum, m/z (absolute intensity) 97 (M + 1, 2624), 96 (M^+, 41472).

Mixture: mass spectrum, m/z (absolute intensity) 98 (4456), 97 (63232), 96 (16112).

2,3-Benzo-6,6-difluorobicylo[3.1.0]hex-2-ene (23).[41]

Into a 100ml round bottom flask with reflux condenser and magnetic stir bar under argon was placed 4.65g (13.4mmol) of $PhHgCF_3$ and 5.72g (38.2mmol) NaI. Each solid was dried overnight on a vacuum line. The NaI was heated at 150°C while drying. Before adding the solids to the flask, they were ground together. In addition, 5.50g (47.4mmol) of freshly distilled dry

(CaH_2) indene and 5ml of dry benzene was added to the solid mixture. The reaction mixture was vigorously stirred and heated at reflux (oil bath at 95°C) for 20 hours. Following the reaction, the mixture was filtered and vacuum transfered. The ^{19}F NMR yield was 41% using hexafluorobenzene as an internal standard. The compound 23 was separated and GC purified utilizing a 20ft Triton X-305 column at 100°C/60psi. The desired compound 23 was characterized as a low melting solid (mp 35-38°C) and 525mg was isolated.

2,3-Benzo-6,6-difluorobicyclo[3.1.0]hex-2-ene (23): ^1H NMR δ 7.35 (m, 1H, aromatic), 7.18 (m, 3H, aromatic), 3.10-3.40 (m, 2H, $-CH_2-$; m, 1H, cyclopropyl), 2.45 (p, 1H, cyclopropyl); ^{19}F NMR, o = -128.2 (ddd, $^2J_{FF}$ = 151.5 Hz, $^3J_{cisHF}$ = 10.3 Hz, $^3J_{cisHF}$ = 12.2 Hz), -153.8 (dd, $^2J_{FF}$ = 151.4 Hz, $^3J_{transHF}$ = 1.5 Hz); ^{13}C NMR, δ 143.2 (d, aromatic quaternary, $^3J_{CF}$ = 5.5 Hz), 137.0 (s, aromatic quaternary), 127.0 (s, aromatic), 126.7 (s, aromatic), 124.9 (s, aromatic), 124.5 (s, aromatic), 113.0 (dd, $^1J_{CF}$ = 280.5 Hz, $^1J_{CF}$ = 280.7 Hz), 35.4 (dd, cyclopropyl, $^2J_{CF}$ = 12.9 Hz), 31.9 (d, $-CH_2$, $^3J_{CF}$ = 2.2 Hz), 27.1 (dd, cyclopropyl, $^2J_{CF}$ = 10.2 Hz, $^2J_{CF}$ = 10.1 Hz); mass spectrum: m/z (% relative intensisty) 166 (M^+, 14.74), 146 (100.00), 85 (17.78), 71 (25.30), 57 (51.39), 43 (80.26).

Thermolysis of 2,3-Benzo-6,6-difluorobicycl[3.1.0]hex-2-ene (24).

The kinetic vessels were sealed melting point capillaries. A "mother" solution was prepared by adding approximately 5mg of starting material 24 to 0.5ml of the appropriate solution media. Runs were monitored in acetone (n-decane internal standard), buffered acetic acid, n-heptane (n-decane) and DMF.

The buffered acetic acid was prepared by combining freshly distilled acetic acid (5ml), sodium acetate 0.265g: 2.50 mmol) and freshly distilled acetic anhydride (0.306g: 3.0 mmol). The capillaries were pyrolyzed in a Statim-type isothermal heater at 140.0, 150.0, 160.0, 170.0 and 180.0°C in acetone; 81.0, 100.0 and 119.0°C in acetic acid; 186.0 and 70.0°C in n-heptane and DMF respectively. The reactions were followed by GC with a J & W Scientific MEGABORE™ column at lower temperatures (50-100°C) to avoid rearrangements on the column. In each case one product was observed by GC and the raw kinetic data for each solvent run is presented in Table 4-5. The rate constants are reported in Table 3-1.

2-Fluoronaphthalene (25): ^{19}F NMR o = -115.4 (dd, $^{2}J_{HF}$ = 8.7 Hz, $^{2}J_{HF}$ = 8.6 Hz).

Indene-d_1.

Into 250ml round bottom flask charged with a 50ml pressure-equalizing addition funnel, reflux condenser, stopper and magnetic stir bar under nitrogen was placed 40ml of dry THF and 45ml (2.5M/hexane: 110.0mmol) n-butyllithium. The flask was cooled to 5-10°C. Freshly distilled dry (CaH_2) indene (11.6g: 100.0mmol) was introduced to the addition funnel and added slowly while maintaining the temperature. Following the addition a reddish-orange homogeneous solution of indenyllithium resulted. The reaction mixture was warmed to room temperature and then heated at 50°C for 45 minutes. After heating, the indenyllithium was cooled to 0-5°C and transferred via cannula to a

250ml pressure-equalizing addition funnel under nitrogen. The funnel was fitted to another 250ml round bottem flask with a mixture of 10g D_2O and 15g 20% DCl stirring at 0-5°C. The indenyllithium was added slowly, then the flask was allowed to warm to room temperature. The organic layer was separated and 7.7g of deuterated product was isolated after distillation (80°C, 20mm). A mass spectral analysis of the deuterated indene (17 eV) showed the desired compound indene-d_1 (mw 117) was 81% of the product mixture. Undeuterated material (mw 116) was present in 8% while dideuterated compounds (mw 118) were observed in 11%. A mass spectrum of pure indene (17 eV) was used to make the appropriate quantitative corrections (eg. ^{13}C content). The total yield of the desired compound (indene-d_1) was 66.0%.

<u>endo and exo-2,3-Benzo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene (41 and 42)</u>.[41]

The standard apparatus for the carbene addition previously described in the undeuterated case was used. Into the apparatus was placed the ground dry solids $PhHgCF_3$ (7.24g: 20.9mmol) and NaI (9.41g: 62.8mmol). Also 7.36g (62.8mmol) deuterated indene and 10ml benzene were added and stirred at 80°C for 15 hours. The ^{19}F NMR yield was 31.8% and 547 mg was isolated pure by preparative GC.Impurities in starting material were accounted for by examining the thermolysis products by mass spectrometry.

<u>endo and exo-2,3-Benzo-4-deuterio-6,6-difluorobicylo[3.1.0]hex-2-ene (41 and 42)</u>: ^1H NMR δ 7.05-7.41 (m, 4H, aromatic), 3.04-3.43 (m, 2H, CHD + cyclopropyl), 2.45 (m, 1H, cyclopropyl); ^{19}F NMR o = -127.9 (dm, $^2J_{FF}$ = 154.0

Hz), -153.7 (d, $^{2}J_{FF}$ = 153.7 Hz).

Thermolysis of a 50:50 Mixture of 41 and 42.

The controled pyrolysis of the mixture was carried out in a sealed 507 NMR tube in acetone-d_6 solution at 150.0°C. A total of 10mg of starting materials was pyrolyzed. At 20% conversion, a ^{1}H NMR spectrum confirmed the ratio of starting materials was unchanged (essentially 1:1). The integration at δ 3.33 was 0.4547. At time zero this integration was 0.4541. This chemical shift represents one of the methylene protons and integrates to one in the undeuterated system. The 20% pyrolysis products were seperated using preparative GC at 50°C and 60psi. Also the injector and detector were each set at 50°C to insure no rearrangement. The product peak contained deuterated 2-fluoronaphthalene and undeuterated 2-fluoronaphthalene. This solid sample was submitted along with pure 2-fluoronaphthalene for quantitative low voltage (17eV) mass spectrometry. Corrections were made for un- and dideuterated material which existed in the indene starting material. The ratio of 4-deuterio-2-fluoronaphthalene to 2-fluoronaphthalene was determined to be 1.31:1.00. Another sample pyrolyzed to a half-life was subjected to the same analysis. The ^{1}H NMR methylene peak integrated to 0.4534 and the MS analysis gave a ratio of 1.15:1.00.

2-Fluoronaphthalene: mass spectrum, m/z (absolute intensity) 147 (M + 1, 1407), 146 (M^{+}, 13595), 145 (M - 1, 1273).

Mixture: mass spectrum, m/z (absolute intensity) 148 (4144), 147

(25387), 146 (20980), 145 (2591).

2,3-Benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene (37).[41]

Once again, into the standard apparatus was placed 2.84g (8.20mmol) $PhHgCF_3$ and 3.60g (24.0mmol) NaI. The olefin 1,2-dihydronaphthalene (10ml: 9.96g) was syringed into the reaction flask purged with nitrogen. No benzene solvent was added. The reaction was run neat in excess olefin at 80°C for 20 hours. Following the reaction, the starting material and product were filtered and the ^{19}F NMR yield was determined to be 38.2%. Preparative GC allowed for the isolation of approximately 500mg of the pure clear liquid product.

2,3-Benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene (37): ^1H NMR δ 6.96-7.43 (m, 4H, aromatic), 2.46-2.90 (complex m, 2H, benzylic-CH_2; 1H, CH), 1.93-2.32 (complex m, 1H, CH; 1H, cyclopropyl), 1.71 (m, 1H, cyclopropyl); ^{19}F NMR o = -118.4 (ddd, $^2J_{FF}$ = 154.3 Hz, $^3J_{cisHF}$ = 13.3 Hz, $^3J_{cisHF}$ = 13.9 Hz), -145.8 (d, $^2J_{FF}$ = 154.7 Hz); ^{13}C NMR, δ 135.0 (d, quaternary, $^3J_{CF}$ = 2.1 Hz), 129.8 (s, aromatic), 128.8 (s, aromatic), 126.6 (s, aromatic), 126.2 (s, aromatic), 114.4 (dd, $^1J_{CF}$ = 289.5 Hz, $^1J_{CF}$ = 289.3 Hz), 26.4 (d, -CH_2, $^3J_{CF}$ = 6.8 Hz), 25.2 (dd, $^2J_{CF}$ = 12.2 Hz, $^2J_{CF}$ = 12.6 Hz), 22.5 (dd, $^2J_{CF}$ = 10.2 Hz, $^2J_{CF}$ = 10.1 Hz), 15.2 (s, benzylic-CH_2); mass spectrum: m/z (% relative intensity) 181 (M + 1, 16.49), 180 (M^+, 87.11), 179 (M - 1, 26.22), 165 (24.56), 159 (32.11), 152 (40.30), 130 (62.02), 129 (100.00), 128 (73.75), 115 (58.13).

Acetolysis of 2,3-Benzo-7,7-difluorobicyclo[4.1.0]hept-2-ene (37).

The kinetic vessels were sealed 507 NMR tubes and the reactions were

followed by ^{19}F NMR. The solvent solution was prepared by adding 1.5ml $CDCl_3$ and 0.05g hexafluorobenzene to 5ml of the standard acetic acid buffer. The tubes were pyrolyzed in the Statim type isothermal heater at 191.0, 204.0 and 217.0°C. The raw kinetic data from quantitative ^{19}F NMR integration may be found in Table 4-6, and rate constants are presented in Table 3-2. Two products, formed competitively (about 50:50), were observed and characterized by ^{19}F NMR as derived from HF elimination and acetate trapping.

trans-1,1-Difluoro-2-methyl-3-phenylcyclopropane (38).[32]

The standard procedure and apparatus was used in the synthesis of 38. Beta-methylstyrene (0.97g: 7.6mmol), 1.48g (22.8mmol) zinc with 10ml THF was placed into the reaction flask. Into a pressure-equalizing addition funnel was placed 4.78g (22.8mmol) CF_2Br_2 in 15ml THF. The yield of 38 by ^{19}F NMR was 31.4%. The clear, pure liquid was isolated (378mg) by preparative GC.

trans-1,1-Difluoro-2-methyl-3-phenylcyclopropane (38): ^1H NMR δ 7.27 (complex m, 5H, aromatic), 2.28 (dd, $^3J_{cisHF}$ = 13.2 Hz, $^3J_{HH}$ = 5.6 Hz), 1.84 (d of quintets ?, $^3J_{cisHF}$ = 13.0 Hz), 1.35 (dm, 3H, methyl); ^{19}F NMR o = -137.9 (dd, $^2J_{FF}$ = 153 Hz, $^3J_{cisHF}$ = 13.0 Hz), -138.9 (dd, $^2J_{FF}$ = 153 Hz, $^3J_{cisHF}$ = 13.5 Hz); mass spectrum, m/z (relative intensity) 169 (M + 1, 17.56), 168 (M^+, 94.02), 167 (M - 1, 12.21), 153 (100.00), 133 (85.46), 117 (76.09).

Thermolysis of trans-1,1-Difluoro-2-methyl-3-phenylcyclopropane (38)

The standard acetic acid buffer was used to examine the acetolysis of 38 in a sealed 507 NMR tube. The reaction was followed at 217.0°C and with hexafluorobenzene as the internal standard. The one major product of the

acetolysis was not characterized. The quantitative integrations of starting material and internal standard are presented in Table 4-7 while the rate constant at 217.0°C is reported in Table 3-2.

<u>endo and exo-2,3-Benzo-6-chloro-6-fluorobicyclo[3.1.0]hex-2-ene (39) (40)</u>.[42]

A 100ml, three-necked, round bottom flask was equipped with a magnetic stirrer, thermometer, rubber septum with nitrogen inlet needle and a pressure-equalizing addition funnel with nitrogen outlet. The flask with 30ml THF was cooled in a salt-ice bath and then 4.33g (22.8mmol) $TiCl_4$ was added at such a rate to keep the temperature below 5°C. A yellow precipitate was formed. Another addition funnel was introduced containing a solution of 0.91g (22.8mmol) $LiAlH_4$ in 20ml THF. This solution was carefully added with the temperature remaining below 15°C. The reaction mixture turned a dark brown color and was allowed to stir without cooling following the addition for one hour.

The flask was cooled again in a salt-ice bath. At 0°C, 0.88g (7.6mmol) of freshly distilled indene was added. Then a solution of 3.13g (22.8mmol) $CFCl_3$ in 10ml THF was added at such a rate that the temperature remained at 0°C. The mixture was allow to stir for an additional 30 minutes. The reaction mixture was hydrolyzed and the light brown organic layer was dried over magnesium sulfate and then vacuum transfered. The THF present was rotary evaporated, and a viscous, high-boiling, yellow oil was obtained. NMR analysis confirmed the presence of the chlorofluorocyclopropanes in a 2.3:1.0 endo/exo ratio with indene and 2-fluoronaphthalene (a rearrangement product) present as impurities. The ^{19}F NMR yield was 73%.

endo-2,3-Benzo-6-chloro-6-fluorobicyclo[3.1.0]hex-2-ene (39): ^{19}F NMR o = -128.4 (dd, $^{3}J_{cisHF}$ = 16.3 Hz, $^{3}J_{cisHF}$ = 18.8 Hz); mass spectrum: m/z (% relative intensity) 183 (M^{+}, 0.05), 146 (100.00).

exo-2,3-Benzo-6-chloro-6-fluorobicyclo[3.1.0]hex-2-ene (40): ^{19}F NMR o = -162.6 (s, $^{3}J_{transHF}$: v. small); mass spectrum: m/z (% relative intensity) 183 (M^{+}, 0.37), 182 (M - 1, 0.87), 181 (M - 2, 1.16), 148 (10.97), 147 (100.00), 146 (44.05).

Thermolysis of the endo and exo systems (39) and (40).

The pyrolysis of both isomers occured in acetone-d_6 solution in sealed 507 NMR tubes without separating and purifying each isomer. Approximately 5mg of the isomeric mixture was added to each tube. The endo- isomer was studied at 39.0, 49.0 and 63.0°C. The exo- isomer remained stable and did not react over this temperature range. The reaction was followed by ^{19}F NMR and a first-order conversion to 2-fluoronaphthalene via HCl elimination was observed. Quantitative starting material and product integration provided the raw kinetic data reported in Table 4-8.

The pyrolysis of the exo- isomer required higher temperatures and was observed at 140.0, 150.0 and 160.0°C against hexafluorobenzene as an internal standard. The sole pyrolysis product was 2-chloronaphthalene (no increase in 2-fluoronaphthalene observed). The quantitative integrations of starting material and internal standard are listed in Table 4-9. Rate constants for both thermolysis processes are found in Table 3-3.

2-Chloronaphthalene: mass spectrum: m/z (% relative intensity) 164 (M + 2, 32.89), 163 (M + 1, 11.26), 162 (M^{+}, 100.00), 127 (40.56).

Table 4-1. Raw Kinetic Data for the Gas Phase Thermolysis of (22).

Time (min)	(22)	Int. Standard
Temperature: 74.00°C		
0	13.13	54.97
135	12.97	57.34
200	31.02	58.51
335	12.16	54.66
1115	13.62	68.34
Temperature: 96.00°C		
0	41.39	100.0
30	22.69	56.76
68	21.52	58.09
110	21.69	61.61
152	19.76	62.56
200	20.33	66.82
252	17.65	62.09
Temperature: 105.50°C		
0	20.03	55.86
30	18.92	60.64
60	16.75	62.81
100	13.42	58.47
145	13.13	68.58
200	8.289	62.50

Table 4-1.--continued

Temperature: 114.75°C

Time (min)	(22)	Int. Standard
0	11.04	42.27
20	9.438	39.94
45	8.562	43.36
70	6.419	42.61
100	4.995	44.71
Temperature: 123.25°C		
0	10.10	45.29
9	9.529	43.58
20	8.677	47.53
30	6.825	47.20
45	5.124	44.47
65	3.634	45.20
Temperature: 131.25°C		
0	13.98	47.00
6	12.43	45.63
13	9.675	54.39
20	7.117	47.71
30	4.547	53.71
40	3.131	49.80
50	2.131	60.81

Table 4-2. Raw Kinetic Data for the Solution Thermolyses of (22)

n-Hexane

Temperature: 76.0°C

Time (min)	(22)	(24)
0	76.16	23.84
25	72.57	27.43
45	69.05	30.95
65	67.82	32.18
85	65.55	34.45
110	62.16	37.84
Temperature: 93.0°C		
0	82.88	17.12
17	78.85	21.15
27	74.82	25.18
37	72.34	27.66
44	70.00	30.00
52	68.44	31.56
Temperature: 104.0°C		
0	69.00	31.00
5	66.07	33.93
10	61.94	38.06
15	60.16	39.84
20	56.29	43.71
25	53.58	46.42

Table 4-2.--continued

Acetone

Temperature: 75.0°C

Time (min)	(22)	(24)
0	81.98	18.02
7	81.64	18.36
17	80.00	20.00
27	78.47	21.53
35	76.23	23.77
45	75.10	24.90
Temperature: 82.0°C		
0	80.45	19.55
10	77.43	22.57
20	74.09	25.91
36	69.24	30.76
44	66.01	33.99
Temperature: 93.0°C		
0	75.10	24.90
5	72.01	27.99
10	65.68	34.32
17	60.62	39.38
22	52.67	47.33
28	47.23	52.77

Table 4-2.--continued

DMF

Temperature: 82.0°C

Time (min)	(22)	(24)
0	41.20	58.80
10	24.19	75.81
14	18.22	81.78
18	12.12	87.88
22	7.066	92.93

Table 4-3. Raw Kinetic Data for the Thermolysis of (33) and (22).

Time (min)	(33)	Int. Standard
Temperature: 92.80°C		
0	1.08	1.00
60	41.36	39.68
120	39.01	40.08
180	37.81	40.44
246	36.41	41.94
300	37.08	46.09
Temperature: 108.00°C		
0	17.06	43.32
42	14.38	44.34
80	11.56	43.81
120	9.134	44.16
160	6.559	44.60
222	4.156	43.34
Temperature: 125.75°C		
0	36.80	100.0
17	13.84	44.05
45	8.655	39.23
75	5.799	40.87
100	3.755	40.42
120	2.609	41.35

Table 4-3.--continued

Temperature: 92.80°C

Time (min)	(22)	Int. Standard
0	1.52	1.00
40	47.12	31.19
60	46.41	32.48
81	44.04	32.55
120	39.16	31.91
160	35.55	31.54
205	28.32	31.67
Temperature: 108.00°C		
0	39.17	16.79
20	36.89	17.87
40	31.27	18.42
60	28.48	17.39
80	26.37	18.79
100	21.56	18.47
Temperature: 125.75°C		
0	18.41	49.02
8	15.10	49.78
17	13.49	60.78
26	9.610	58.28
34	8.075	62.54

Table 4-3.--continued

Acetone

Temperature: 84.0°C

Time (min)	(33)	(36)	(22)	(24)
0	76.22	23.78	78.22	21.78
45	70.04	29.96	75.34	24.66
90	63.92	36.08	72.49	27.51
120	57.41	42.59	69.51	30.49
165	51.82	48.18	66.44	33.56

Table 4-4. Raw Kinetic Data for Thermolysis of (34) and (35).

Acetone

Temperature: 93.0°C

					Products	
Time (min)	(34)	(35)	IS	m	p	o
0	8.814	9.611	81.58	--	--	--
5	7.431	8.082	81.89	1.20	--	--
14	6.607	6.811	81.38	2.29	--	--
25	4.118	4.328	81.65	5.90	0.94	--
30	3.593	3.609	81.19	7.85	1.52	--
420	---	---	90.01	8.06	1.42	0.516

Table 4-5. Raw Kinetic Data for the Thermolysis of (23).

Acetone

Temperature: 140.0°C

Time (min)	(23)	Int. Standard
0	32.52	40.19
30	10.39	15.95
60	5.544	13.55
90	4.626	14.91
120	3.204	14.26
150	1.722	15.97
Temperature: 150.0°C		
0	96.26	100.00
40	27.53	30.72
60	31.10	36.39
80	26.59	31.63
100	27.16	35.32
120	26.70	35.14
140	16.77	23.23
160	24.25	34.42
181	19.77	29.25

Table 4-5.--continued

Temperature: 160.0°C

Time (min)	(23)	Int. Standard
0	96.26	100.0
15	29.69	32.10
30	32.06	36.63
60	25.72	32.96
90	14.54	20.90
120	22.63	36.80
135	12.44	24.06
Temperature: 170.0°C		
0	26.06	34.57
10	26.93	30.79
25	24.76	33.04
35	22.11	30.07
50	18.48	28.77
60	13.71	21.74
75	16.49	30.77
85	21.21	40.14
100	15.16	34.04
110	7.720	18.65

Table 4-5.--continued

Temperature: 180.0°C

Time (min)	(23)	Int. Standard
0	26.06	34.57
5	30.78	41.59
10	27.10	38.76
23	19.76	34.31
30	23.01	43.49
36	16.81	34.89
44	16.62	41.69
n-Hexane Temperature: 186.0°C		
0	2.219	1.326
110	1.970	1.258
220	1.302	1.129
330	0.9887	1.136
430	0.6347	1.244
480	0.6370	1.356
DMF Temperature: 70.0°C		
0	5.805	0.6245
104	6.470	0.9827
155	6.642	1.187
180	8.009	1.573
200	6.111	1.265
220	7.117	1.564

Table 4-5.--continued

Acetic Acid: Temperature: 81.0°C

Time (min)	(23)	(25)
0	1.096	----
5	1.173	0.0653
10	0.9633	0.0583
15	1.070	0.0740
24	1.026	0.0857
30	0.9350	0.0890
Temperature: 100.0		
0	1.050	----
5	0.9223	0.09300
10	0.8733	0.1377
15	0.8443	0.1713
20	0.7860	0.2213
25	0.7380	0.2560
Temperature: 119.0°C		
0	1.044	----
3	0.8120	0.1880
6	0.6803	0.3127
9	0.5973	0.4857
12	0.5037	0.5653
15	0.3987	0.6417
18	0.3297	0.6767

Table 4-6. Raw Kinetic Data for the Acetolysis of (37).

Temperature: 191.0°C

Time (min)	(37)	Int. Standard
0	60.71	39.29
30	58.94	41.06
55	58.63	41.37
106	58.05	41.95
131	57.68	42.32
191	57.06	42.94
Temperature: 204.0°C		
0	38.09	61.91
15	36.75	63.25
30	36.21	63.79
45	36.06	63.94
75	34.10	65.90
90	33.68	66.32
130	28.82	71.18
Temperature: 217.0°C		
0	51.74	48.26
25	46.79	53.21
40	44.13	55.87
55	42.88	57.12
65	41.23	58.77
75	40.54	59.46

Table 4-7. Raw Kinetic Data for the Acetolysis of (38).

Temperature: 217.0°C

Time (min)	(38)	Int. Standard
0	46.29	53.71
15	46.20	53.80
31	43.58	56.42
46	39.24	60.76
58	36.75	63.25
68	35.47	64.53
83	32.44	67.56

Table 4-8. Raw Kinetic Data for the Thermolysis of (39).

Temperature: 39.0°C

Time (min)	(39)	(25)
0	65.54	34.46
6	65.01	34.99
14	64.24	35.76
21	63.71	36.28
28	63.00	37.00
Temperature: 49.0°C		
0	68.60	31.40
7	65.78	34.22
12	63.52	36.48
17	61.66	38.34
22	59.41	40.59

Table 4-8.--continued

Temperature: 63.0°C

Time (min)	(39)	(25)
0	24.00	76.00
4	21.80	78.20
12	16.66	83.34
16	14.74	85.26
21	12.14	87.86

Table 4-9. Raw Kinetic Data for the Thermolysis of (40).

Temperature: 140.0°C

Time (min)	(40)	Int. Standard
0	35.52	64.48
6	32.61	67.39
11	31.28	68.72
17	29.05	70.95
23	27.00	73.00
28	26.91	73.09
33	23.59	76.41
Temperature: 150.0°C		
0	34.63	65.37
8	27.29	72.71
13	23.20	76.80
18	20.95	79.05
23	18.15	81.85
28	15.38	84.62
33	12.96	87.04

Table 4-9.--continued

Temperature: 160.0°C

Time (min)	(40)	Int. Standard
0	36.45	63.55
5	26.31	73.69
8	21.55	78.45
11	18.39	81.61
14	15.66	84.34
17	12.54	87.46
20	10.97	89.03

APPENDIX
SELECTED SPECTRA

The ^{1}H, ^{2}H, ^{19}F and ^{13}C NMR spectra of new compounds are depicted graphically in this appendix. The spectral data have been transcribed and are presented in numerical form in Chapter 4. In some cases, sample spectra of thermolysis processes are included. The 6,6-difluorobicyclo [3.1.0]hex-2-ene systems discussed in Chapter 2 are given in Figures A-1 through A-7. The benzo-dihalobicyclic systems presented in Chapter 3 follow in Figures A-8 through A-19.

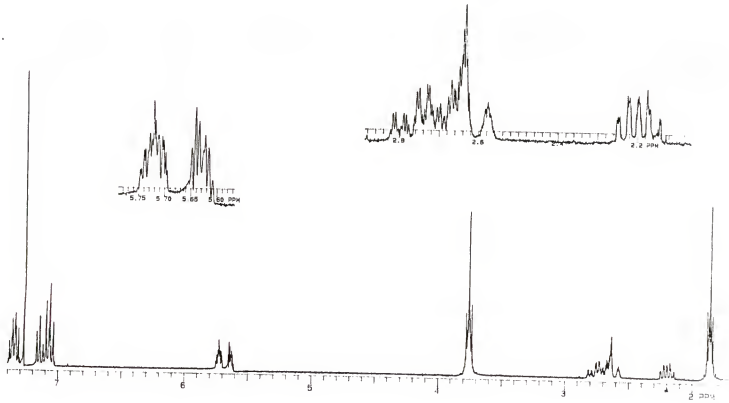


Figure A-1. 300 MHz ^{1}H Spectrum of 22.

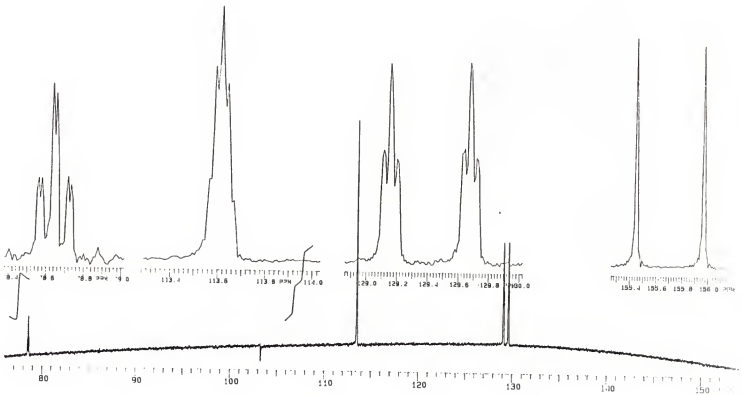


Figure A-2. 300 MHz ^{19}F Spectrum of 22.

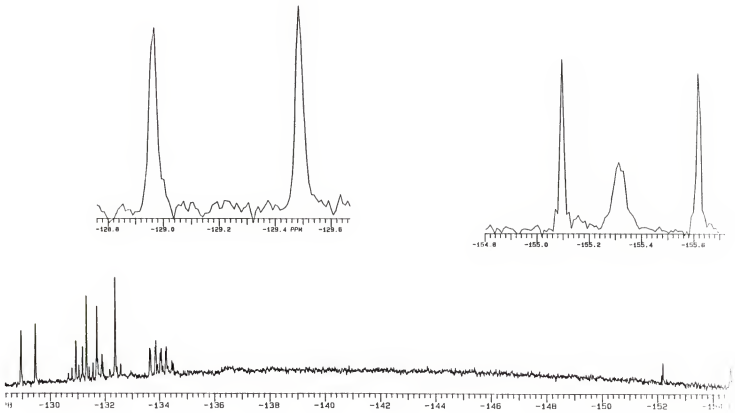


Figure A-3. 300 Mhz ^{19}F Spectrum of 33.

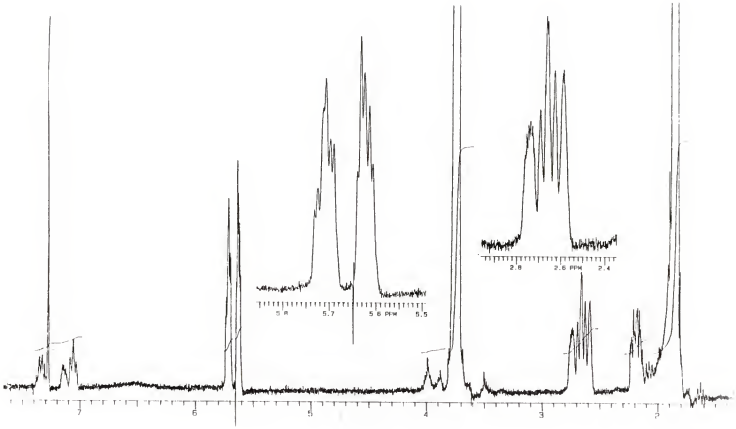


Figure A-4. 300 Mhz ^{1}H Spectrum of 34 and 35.

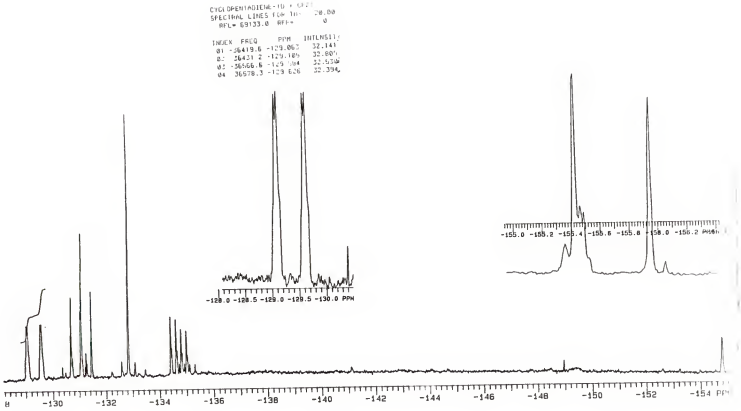


Figure A-5. 300 Mhz ^{19}F Spectrum of 34 and 35.

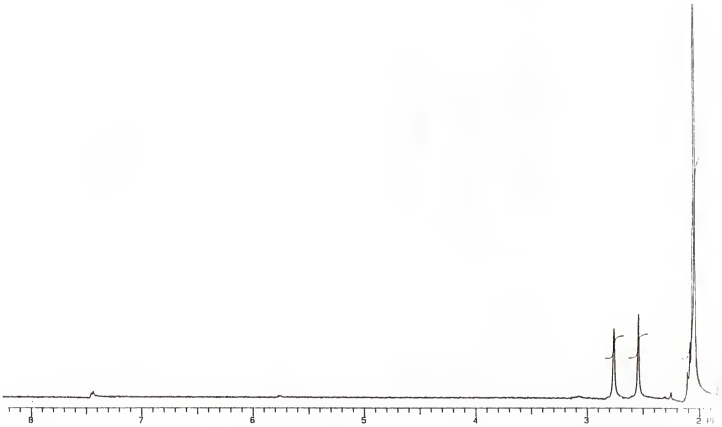


Figure A-6. 300 Mhz ^{2}H Spectrum of 34 and 35.

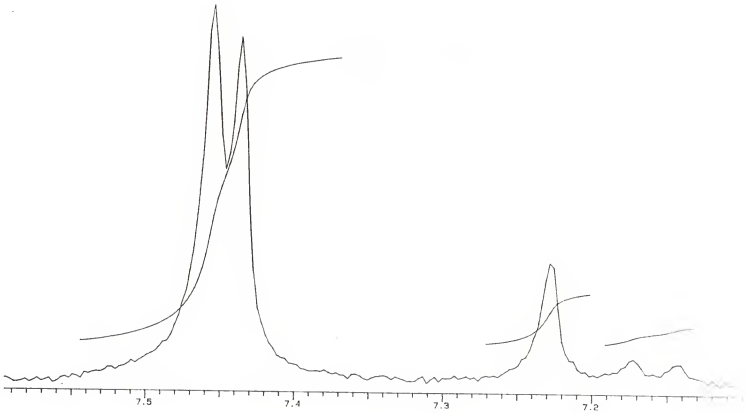


Figure A-7. 300 Mhz ^{2}H Spectrum of o, p, m-deuteriomonofluorobenzenes

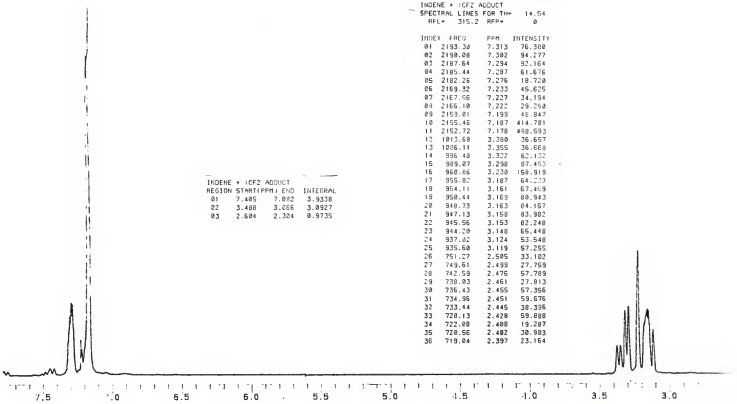


Figure A-8. 300 Mhz ^{1}H Spectrum of 23.

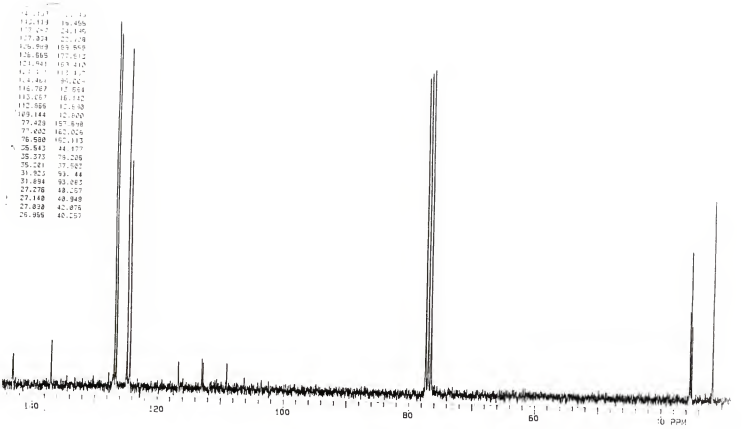


Figure A-9. 300 Mhz ^{13}C Spectrum of 23.

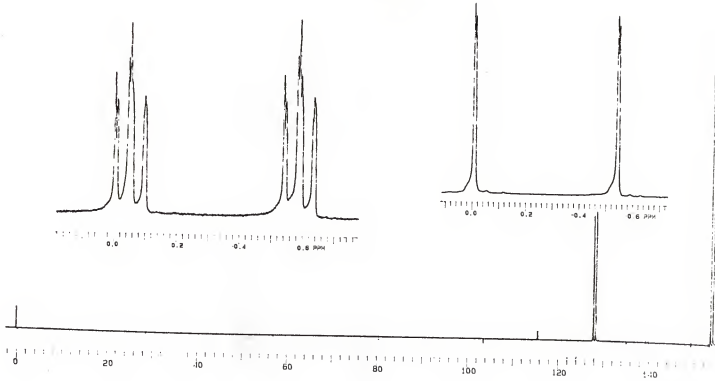


Figure A-10. 300 Mhz ^{19}F Spectrum of 23.

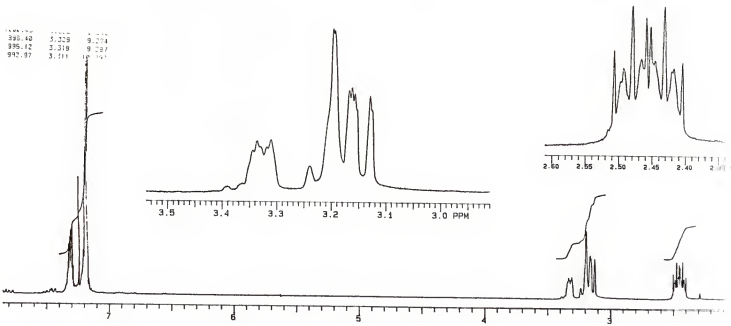


Figure A-11. 300 Mhz ^{1}H Spectrum of <u>endo</u>- and <u>exo</u>-2,3-benzo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene.

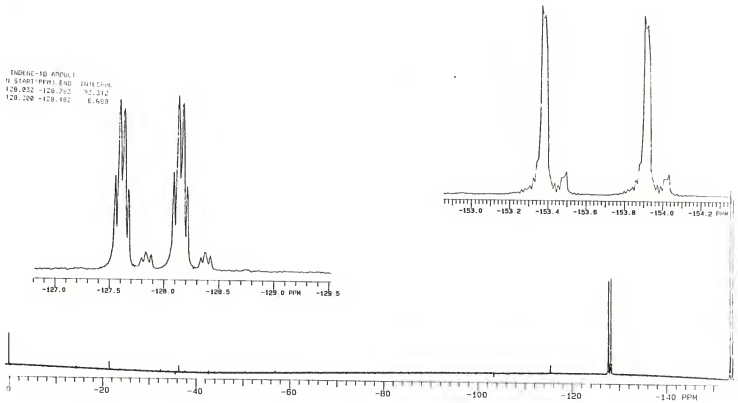


Figure A-12. 300 Mhz ^{19}F Spectrum of <u>endo</u>- and <u>exo</u>-2,3-benzo-4-deuterio-6,6-difluorobicyclo[3.1.0]hex-2-ene.

:CF2
CTRAL LINES FOR TH= 10.65
FL= 329.2 RFP= 0

NEX	FREQ	PPM	INTENSITY
1	2179.71	7.268	33.793
2	2177.06	7.259	23.823
3	2173.93	7.248	47.976
4	2170.54	7.237	69.534
5	2155.97	7.188	125.778
6	2151.93	7.175	95.082
7	2150.79	7.171	125.810
23	2146.99	7.159	129.351
28	2133.93	7.115	52.576
10	2127.52	7.094	39.631
11	2121.98	7.075	25.663
12	912.00	2.727	62.819
13	807.61	2.693	44.284
14	803.95	2.681	61.275
15	809.53	2.669	86.963
16	798.82	2.663	92.475
17	793.82	2.644	27.767
18	797.59	2.626	71.986
19	646.52	2.156	23.851
20	644.83	2.147	37.021
21	640.96	2.137	35.410
22	640.12	2.134	32.316
23	638.41	2.129	30.738
24	637.85	2.124	24.336
25	634.94	2.117	26.856
26	633.72	2.113	21.483
27	631.62	2.107	25.895
28	626.99	2.091	20.788
29	514.14	1.714	28.624
30	506.09	1.634	20.148
31	0.92	0.003	134.367

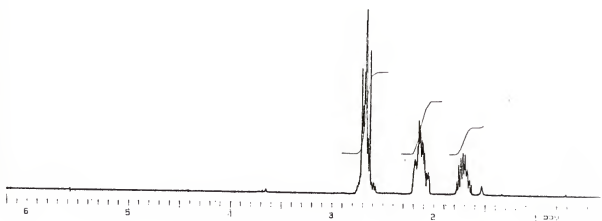


Figure A-13. 300 Mhz ^{1}H Spectrum of 37.

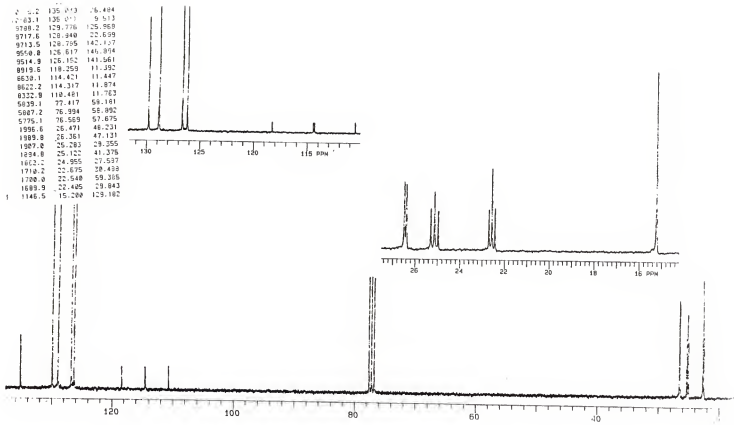


Figure A-14. 300 Mhz ^{13}C Spectrum of 37.

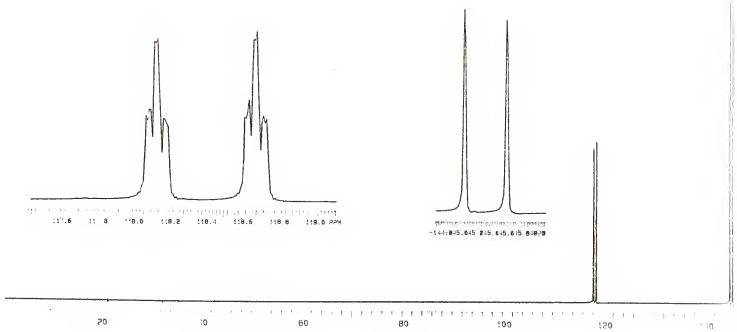


Figure A-15. 300 Mhz ^{19}F Spectrum of 37.

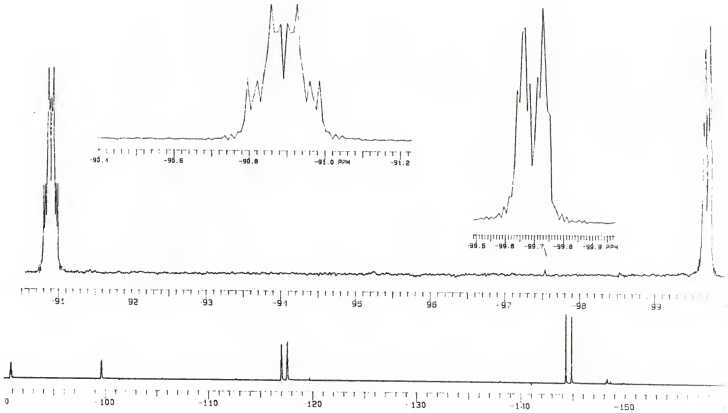


Figure A-16. 300 MHz ^{19}F Spectrum of the thermolysis of 37.

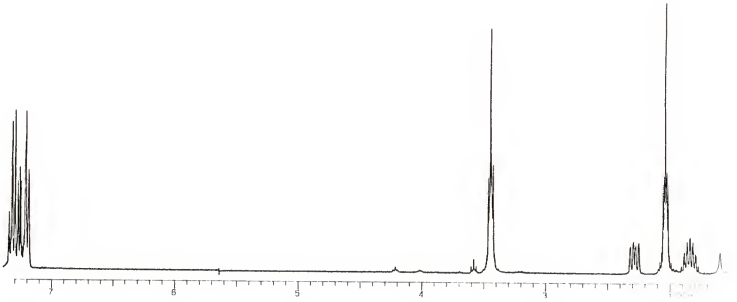


Figure A-17. 300 Mhz ^{1}H Spectrum of 38.

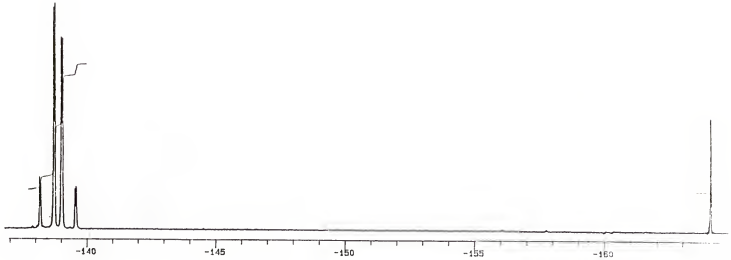


Figure A-18. 300 Mhz ^{19}F Spectrum of 38.

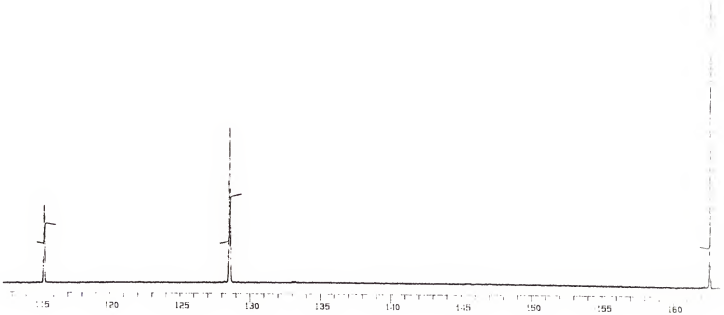


Figure A-19. 300 Mhz ^{19}F Spectrum of 39 and 40.

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BIOGRAPHICAL SKETCH

Jeffrey J. Keaffaber was born November 20, 1962, the first of three boys who have, over the years, constantly tried the everlasting patience of their mother, Diana. Early in life, Jeff developed his skills in baseball, golf and other outdoor activites in addition to "studying." Jeff attended Manchester College in Indiana to study chemistry and biology. It was here his love for science, especially chemistry, was realized. At Manchester, he received diligent nurturing from Dr. Ed Miller who insured his pursuance of graduate school. After graduating with distinction in May, 1985, Jeff began graduate studies in August 1985 at the University of Florida where he is now a candidate for the Ph.D. degree in December, 1989. During his short time in Gainesville, Jeff came to know his best friend and first love, Lisa. Upon completion of his doctoral studies, Jeff will continue his interests in running and horses and start working for the Walt Disney Co./Epcot Center research facilities in Orlando, Florida.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

William R. Dolbier, Jr., Chairman
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

William M. Jones
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Kirk S. Schanze
Assistant Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Philip Brucat
Assistant Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Cliff Johnston
Assistant Professor of Soil Science

This dissertation was submitted to the Graduate Faculty of the Department of Chemistry in the College of Liberal Arts and Sciences and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

December 1989

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Dean, Graduate School